When we move together

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When We Move Together:
The Neural Correlates of Joint Action

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1. Introduction

The well-known movie *Modern Times (1936)* caricaturizes how being forced to act/work in isolation can influence the human condition. In the movie, Charlie Chaplin casts a "modern" factory worker who is employed on an assembly line. In one shot, we see him tightening bolts in the company of several co-workers. In a next shot, the assembly line speeds up tremendously and he works with great effort, struggling miserably, but nobody comes to help him. In another shot, he is being fed by an automatic feeding machine introduced by the employers. At the end, Charlie experiences a mental breakdown due to social alienation. Indeed, during the 1930's, when "modern" working conditions reduced the likelihood of social interactions between workers, many of them began to suffer from isolation (Frisby, 1987; Marx, 1973).

In contemporary Western societies, regardless of claims about their individualistic orientation, many aspects of everyday life are fundamentally based on socially coordinated actions of human beings. With a quick gaze around us, we may see many socially coordinated actions performed almost effortlessly, ranging from two friends jointly carrying a heavy table to sports teams that skillfully coordinate their movements to defeat their adversaries, to musicians playing together in an orchestra. These types of actions, performed by two or more individuals who coordinate their actions in space and time to bring about a change in the environment, are often referred to as joint actions (Sebanz et al., 2006a). Although joint actions play an important role in many everyday activities and are at the core of our ability to cooperate, the question of how we accomplish these seemingly simple actions remains an issue of debate in social neuroscience.

The neural systems recruited while participants observe the actions of others and execute actions by themselves have been explored extensively (Buccino et al., 2004; Chong et al., 2008; Gazzola et al., 2007; Iacoboni, 2005; Iacoboni et al., 1999; Kilner et al., 2009; Rizzolatti and Craighero, 2004; Rizzolatti et al., 1996a; Rizzolatti et al., 1996b; Rizzolatti et al., 2001). However, during most social interactions, there is not a single actor and a single observer; instead individuals are simultaneously observers as well as actors who need to adjust their own actions to those of others (Keysers and Fadiga, 2008). Recently, the interest in this reciprocal nature of social interactions and its underlying neural processes has surged. Researchers increasingly try to tackle the difficult question of how interactions between self-propelled agents unfold in space and time by probing the brain activity of humans (Kokal et al., 2009; Newman-Norlund et al., 2008; Newman-Norlund et al., 2007b; Schippers et al., 2009; Sebanz et al., 2006b; Sebanz et al., 2007) and monkeys (Fijii et al., 2008).

Likewise, this thesis aimed at advancing the present knowledge on the neural signature of social interactions, in particular during joint actions, in humans. We first present two functional magnetic resonance imaging (fMRI) experiments (Experiment 1 and 2) exploring the neural mechanisms involved in joint actions when two agents mutually coordinate their actions while playing a cooperation game (Chapter 2). Second, we demonstrate information flow between the brain areas identified in

Experiment 1 by employing an effective connectivity method (Chapter 3). Third, we present an fMRI experiment (Experiment 3) in which we examine the responses of the reward system in the brain during a social drumming task to reveal the rewarding effects of engaging in musical joint actions. In addition, we demonstrate the results of a prosocial commitment test performed immediately after the Experiment 3, which investigates the influence of drumming together on helping behavior between the drum partners (Chapter 4).

1.1. Background Information

Before describing the experiments in detail I will provide a brief overview of the current knowledge about action planning and coordination in social context, the mirror neuron system and joint music making that paved the way for this thesis.

Action Planning and Coordination in Social Context

The mechanisms that enable a single agent to coordinate his or her own actions have been investigated through a variety of experimental paradigms such as task switching and multi-tasking paradigms (Allport, 1993; Mayr and Keele, 2000; Meyer and Kieras, 1997). Results of such studies have shown that individuals do not merely act upon external stimuli but adapt their own actions according to their plans on how to achieve a goal (Bekkering et al., 2000). Importantly, these plans to achieve an action are usually internal to the actor (Allport, 1993; Hommel et al., 2001; Prinz, 1997).

A joint action involves two or more actors who lack insight into each other's mind. When each individual tries to coordinate his/her actions according to his/her own internally generated plans, acting together to achieve a common goal may prove difficult. Consider, for example, a young couple picnicking in the park. If it suddenly starts raining, they would both get up and grasp the heavy picnic basket in order to carry it together to a sheltered place. Although carrying a basket is a simple action, to achieve this goal with another agent is a difficult task as these two agents execute their actions according to their own internally generated action plans. Thus, on the way to the shelter, they will need to coordinate a chain of actions on how to grab the basket and on where and when to walk. Clark (1996) suggested language[1] as a powerful coordinating device for such situations (Clark, 1996). However, as engaging in joint action entails great timing demands, verbal communication between individuals would often be too slow and inefficient.

How is it then possible that individuals can coordinate their actions in space and time to achieve a common goal? Early research revealed that observing others acting affects one's own action planning and control. It has been demonstrated that an individual's performance is facilitated when he/she observes a similar action performed by another individual in the proximity whereas observing the opposite action interferes with performing the same action (Brass et al., 2001; Sturmer et al., 2000). Such effects of the sight of others' actions on one's own performance are

[1] The question of if language itself is a form of joint action is out of the scope of this thesis.

addressed by theoretical frameworks such as ideomotor theory (Greenwald, 1970; James, 1980) and the common coding theory (Hommel et al., 2001; Prinz, 1997). These theories propose that observing actions performed by others might activate the same representations that govern one's own planning and control of these actions because the same representations are involved in action production and observation.

As a first step towards understanding joint action coordination, researchers investigated how individuals perform a task with a co-acting agent using a modified version of a spatial stimulus-response (S-R) compatibility task (Atmaca et al., 2008; Sebanz et al., 2003; Sebanz et al., 2005; Tsai et al., 2008). In a typical spatial stimulus-response (S-R) compatibility task, participants press a left key when they see a red light and a right one when they see a green light and are found to respond less accurately and/or slower to stimuli presented contralateral to the correct response than to stimuli presented on the ipsilateral side (Wallace, 1971). Sebanz and colleagues (2003), for instance, distributed this task among two agents (a participant and a confederate). They then compared the task performance of the participant when he/she acts alongside another agent (group condition) to when he/she performs the identical task alone (Sebanz et al., 2003). Their results demonstrated a spatial compatibility effect[2] in the group condition in which a participant and the confederate performed their own half of the task. More importantly, there was no spatial compatibility effect when participants performed their half of the task alone, although the participant's task was identical to the task in the group condition (Sebanz et al., 2003). Similar group effects were also found when participants knew the confederate's task but did not see the actions of him/her (Sebanz et al., 2005; Tsai et al., 2008). The conclusion of these studies is that when individuals carry out different parts of a task, each actor represent the whole task (both his/her own and the other's) instead of representing only his/her own part of the task. This suggests that we automatically represent potential actions of others just like our own actions when we perform tasks together with others. This automatic tendency ability to form shared action representations are typically referred to as co-representations or shared representations in the literature (Sebanz et al., 2003; Sebanz et al., 2005).

Although these (and other) behavioral studies did not provide empirical evidence of the neural mechanisms underlying co-representations occurring in group settings, they claimed that the MNS may play a role in representing one's own and other's action in a functionally equivalent way when performing a task together with another agent (Atmaca et al., 2008; Sebanz et al., 2006a; Sebanz et al., 2003; Sebanz et al., 2005; Tsai et al., 2008).

Later, neural correlates of shared representations were investigated with an ERP[3] study (Sebanz et al., 2006b). Sebanz and colleagues (2006) compared the ERPs and electrophysiological responses when participants performed a task alone to those when they performed the task together with another individual. Their results demonstrated similar electrophysiological response at frontal brain sites in response to

[2] A typical spatial compatibility effect indicates that task-irrelevant properties of the stimulus (i.e. the location of the stimulus relative to the participant) interfere with performance.

[3] Event-related brain potentials (ERPs) are a non-invasive method of measuring brain activity during cognitive processing.

a stimulus referring to the other's action and to the one referring to one's own action. They suggested that as one's own actions and others' actions were represented in a common domain the mirror neurons system (MNS) might play a role when individuals perform actions in turns with others (Sebanz et al., 2006b).

The Mirror Neuron System and Joint Actions

An accumulating body of studies suggests that perceivers are able to understand the actions of others and the intentions behind these actions while passively observing them (Puce and Perrett, 2003). It has been proposed that seeing actions performed by others may directly trigger motor and somatosensory representations as they would be elicited by one's own actions in similar circumstances (Bastiaansen et al., 2009; Fogassi et al., 2005; Gallese et al., 1996; Gazzola and Keysers, 2009; Keysers et al., 2004; Kilner et al., 2004; Rizzolatti et al., 2001; Umilta et al., 2001). This intriguing mechanism could allow observers to understand the actions of others based on their own experiences and provides 'a first-person grasp of the motor goals' of others (Rizzolatti and Sinigaglia, 2010).

Originally, the idea of such a mechanism emerged from the discovery of mirror neurons in the ventral premotor cortex (area F5) (Pellegrino et al., 1992) and in the parietal cortex (area PFG located between parietal areas PF and PG) (Fogassi et al., 2005) in the monkey brain with a series of single neuron recording experiments. These neurons were called mirror neurons as they displayed a unique response pattern of being equally responsive to both the execution of the actions performed by the monkey itself and the observation of similar actions performed by an experimenter. Single neuron recording is an invasive technique not commonly used in humans. Following these original observations, several studies using different techniques such as fMRI (Buccino et al., 2001; Buccino et al., 2004; Carr et al., 2003; Chong et al., 2008; Gazzola and Keysers, 2009; Gazzola et al., 2007; Iacoboni, 2005; Iacoboni et al., 1999; Kilner et al., 2009; Kokal et al., 2009), PET (Grafton et al., 1996; Rizzolatti et al., 1996b), MEG (Hari et al., 1998), TMS (Avenanti et al., 2007; Catmur et al., 2009; Fadiga et al., 1995) and extracellular recordings (Mukamel et al., 2010) have provided strong converging evidence for the existence of the MNS in the human brain. The ventral and dorsal premotor areas (BA 44 and BA 6), the inferior parietal lobe (IPL), the middle temporal gyrus (MTG), the supplementary motor area (SMA) and the somatosensory cortex have all been identified as being active during both action observation and execution in humans. These structures together are often referred to as the putative MNS (pMNS). The term 'putative' underlines the fact that an increase in BOLD response both during action observation and execution in a voxel can only suggest that it could contain mirror neurons. Alternative explanations, such as that the voxel contains distinct but interdigitated populations of neurons involved in action observation only and execution only are also possible (Keysers and Gazzola, 2009; Kokal et al., 2009).

As the monkey mirror neurons and the putative human equivalent respond to both action observation and execution, it has been claimed that we directly map the observed actions of others on our motor system, typically referred to as the direct-matching hypothesis (Gallese, 1998; Rizzolatti et al., 2001). This hypothesis claims

that the mirror mechanism unifies perception and action by transforming sensory representations of an action into motor representations of the same action in the observer's brain (Rizzolatti and Sinigaglia, 2010). Therefore, it has been suggested that the functional role of the MNS is action understanding as such mapping would allow one to recognize the goals of others using the link between one's own motor acts and their perceptual consequences (Fogassi et al., 2005; Gallese et al., 1996; Iacoboni, 2005; Rizzolatti and Craighero, 2004; Rizzolatti et al., 1996a; Umilta et al., 2001).

It has been suggested that the functional role of the mirror neurons includes many aspects of social cognition such as imitation (Iacoboni et al., 1999), empathy (Bastiaansen et al., 2009; Fogassi et al., 2005; Gallese et al., 1996; Jabbi and Keysers, 2008; Keysers and Gazzola, 2006), mind-reading (Gallese, 2003; Gallese, 1998), gestural communication (Schippers et al., 2009; Schippers et al., 2010) and language (Rizzolatti and Arbib, 1998). Maybe not too surprisingly, a number of empirical studies (Newman-Norlund et al., 2008; Newman-Norlund et al., 2007b; Sebanz et al., 2007) and theoretical proposals (Knoblich and Jordan, 2002; Newman-Norlund et al., 2007a; Sebanz et al., 2006a) have also suggested a fundamental role for the MNS during the engagement in joint actions.

Neural Correlates of Joint Actions

In a typical joint action situation mutually acting with others requires the ability to adjust our actions to those of others (Knoblich and Jordan, 2002). According to several experimental and theoretical proposals (Atmaca et al., 2008; Clark, 1996; Knoblich and Jordan, 2003; Knoblich and Jordan, 2002; Newman-Norlund et al., 2008; Newman-Norlund et al., 2007a; Newman-Norlund et al., 2007b; Pacherie and Dokic, 2006; Sebanz et al., 2006a; Sebanz et al., 2006b; Sebanz et al., 2007) the ability to coordinate our actions with those of others depends upon the MNS, a system which allows the direct mapping of observed actions onto one's own motor representations. Such mapping has been claimed to be sufficient to allow an actor to adjust his or her own action plans to the predicted actions of the respective action partner, leading to a successful joint action (Clark, 1996; Newman-Norlund et al., 2008; Newman-Norlund et al., 2007a; Newman-Norlund et al., 2007b; Sebanz et al., 2006a; Sebanz et al., 2006b). Although these proposals suggest a key role for the MNS in joint actions, we know little about its contribution, due to a scarcity of empirical evidence. Existing literature of empirical studies on joint actions includes several behavioral experiments, an ERP experiment and a few fMRI studies.

Behavioral experiments (Atmaca et al., 2008; Knoblich and Jordan, 2003; Sebanz et al., 2003; Sebanz et al., 2005; Tsai et al., 2008) investigating the performance of co-acting individuals have revealed that the actors form shared task representations, yet have not addressed the neural bases of this phenomenon.

The first empirical attempt to reveal the neural processes involved in co-acting with another actor was an fMRI study by Sebanz and colleagues in 2007 (Sebanz et al., 2007). They asked their participants to perform a go-nogo task with a confederate who was present in the scanner room, sitting next to the participants. Their paradigm included single actor conditions in which the participant responded to one of the two

colors alone and co-action conditions in which the participant responded to one color and the confederate responded to the other one by taking turns. They found brain activity in the inferior and superior parietal lobe and supplementary motor area associated with nogo trials in co-acting condition. They conclude that these activations may be the neural correlates of shared representations triggered by observing a co-actor's actions. Although this study was a pioneer in investigating co-acting individuals in fMRI, the task was based on turn taking instead of the continuous adjustment of actions that typically defines joint actions. Thus, it remains unclear how task sharing facilitates choosing a suitable action at the appropriate time when individuals engage in true joint actions.

Recent empirical studies (Kokal et al., 2009; Kokal and Keysers, 2010; Newman-Norlund et al., 2008; Newman-Norlund et al., 2007b) were designed to investigate the role played by the MNS in joint actions. Some of these studies argued that the MNS might be the key neural locus of coordination during joint actions. However, they failed to directly test the contribution of the MNS because they concluded that the brain activations they observed were located in the MNS without actually locating the MNS of their participants. Newman-Norlund and colleagues (2008), for instance, found that the BOLD signal in the inferior frontal gyrus (IFG) was larger when participants balanced a ball together with another agent (a joint action) than when they balanced the ball alone (Newman-Norlund et al., 2008). The authors interpreted this as an evidence for the direct role of the MNS in joint actions. However, they did not confirm that the activations occurred in areas also demonstrating MNS-diagnostic activity. A common test to demonstrate pMNS activity is to identify regions active while viewing an action (another actor balancing a ball) and performing the motor actions alone (the most straightforward definition of the MNS based on single cell recordings). Likewise, in another experiment Newman-Norlund and colleagues (2007) demonstrated greater BOLD signal in the MNS (right IFG and bilateral IPL) during planning of complementary actions compared to imitative actions (Newman-Norlund et al., 2007b). Given that the IFG as well as the IPL are well known to contain other types of neurons in addition to mirror neurons, from the results of these experiments, it is difficult to interpret whether the brain areas identified are really part of the MNS, and hence whether the MNS contributes to joint actions (Kokal et al., 2009; Thioux et al., 2008).

One of the key features of joint actions, which distinguish them from individual actions, is the necessity to continuously adjust one's own actions to those of others. In many cases joint actions do not involve performing identical actions but rather complementary actions. Importantly, we are able to switch between performing same and complementary actions in seconds. In order to shed more light on the contribution of the MNS for this key feature of joint actions, we performed an fMRI study (Experiment 1) specifically aimed at examining the degree to which this adjustment process occurs within or beyond the MNS.

Our results revealed that a typical joint action requires at least three intertwined processes: observing actions of others, executing one's own actions and a task-dependent integration of observed and executed actions (Kokal et al., 2009). As the MNS is known to transform the sight of actions into motor representations of similar actions (Etzel et al., 2008; Gallese et al., 2004; Iacoboni and Dapretto, 2006; Keysers

and Gazzola, 2006; Liepelt et al., 2008; Rizzolatti and Craighero, 2004), it may play a role in representing both partners' actions in a common code. However, the task usually determines the nature of the integration of the observed and executed action. For example, when carrying a picnic basket with another person this integration can vary from doing the same action (e.g. both people lift the basket together) to doing the opposite of the partner (e.g. one moves forward and the other backward to pass a narrow alley). Given that the mirror neurons in the monkey are known to show a fixed relationship between observed and executed actions (Gallese et al., 1996), this task-dependent redefinition of the visuo-motor integration during joint actions is likely to be performed outside the MNS (Kokal et al., 2009; Kokal and Keysers, 2010). In Chapter 2, we propose a potential alternative network of brain areas underlying this key feature of joint actions.

The MNS and Internal Predictive Models in the Service of Joint Actions

Another challenge for motor control during joint actions is the fact that our visual and motor systems have relatively long latencies (several hundreds of milliseconds) (Adam and Van Veggel, 1991; Michie et al., 1976). It has been suggested that the MNS could contribute to solving the time lag issue by allowing one to anticipate future actions of others that are not yet fully visible (Miall, 2003; Ramnani and Miall, 2004; Umilta et al., 2001; Wolpert et al., 2003).

According to influential action models (Kilner et al., 2007b; Miall, 2003; Wolpert et al., 2003; Wolpert, 2000), the motor system uses two forms of internal models, namely inverse and forward models, while executing actions. It has been proposed that the inverse model maps the relationship between the goals and the motor commands necessary to reach a goal while the forward model maps the relationship between motor commands and the sensory outcomes of a motor action (Miall, 2003). It has been claimed that the MNS may act as both models: the circuit linking the superior temporal sulcus (STS)[4], PF and F5 acting as an inverse model, whereas the circuit linking the F5, PF and STS as a forward model (Gazzola and Keysers, 2009; Miall, 2003).

Wolpert & Ghahramani (2000) demonstrated that individuals continuously compare the actual and predicted consequences of their actions by utilizing these internal models (Wolpert, 2000). These models have also been hypothesized to support making predictions about others' actions in the immediate future (Gazzola and Keysers, 2009; Kilner et al., 2007a; Kilner et al., 2004; Miall, 2003; Wolpert et al., 2003; Wolpert, 2000). In such situations, predictions about the actions of others could be formed by comparing the potential motor commands transformed from observation by utilizing the inverse model through which the visual information is converted to a predicted motor plan. Simultaneously, the sensory outcomes of the observed motor action could be predicted by utilizing the forward model (Ramnani and Miall, 2004; Wolpert et al., 2003).

[4] The STS also contains neurons that respond to action observation, yet they do not discharge during action execution. Therefore, STS cannot be considered part of the MNS.

In Chapter 3 we propose that the MNS, as a predictive device, may be involved in joint actions as part of a forward model to predict the future somatosensory and visual consequences of the observed and executed actions, overcoming the otherwise inevitable neural delays. We provide empirical evidence from effective connectivity analysis demonstrating a predominantly backwards information flow from BA44 to the posterior sites of the MNS (BA 2) and the visual areas (i.e. MOG) during joint actions (Kokal and Keysers, 2010). A similar backwards information flow within the MNS during a gestural communication task, a task employing skills similar to those needed for joint action, has also been recently demonstrated (Schippers and Keysers, 2010).

From Joint Actions to Prosocial Behavior

We humans are the only primates that engage in the special from of joint actions that is synchronizing movements or voices during music making and dancing (Wallin et al., 2000). This proclivity for synchronizing one's own actions with those of others is found across all cultures (Wallin et al., 2000) and emerges very early in childhood (Kirschner and Tomasello, 2009).

Why people enjoy joint music making and dancing across all times and cultures remains an open question. Unlike food or sex, jointly acting in a musical context does not provide any obvious fitness advantage, though may increase fitness through social bonding, akin to grooming in non-human primates. One hypothesis on the original adaptive function of such behavior is that our human ancestors invented joint music making and dance as a tool for supporting group cohesion, ultimately increasing prosocial in-group behavior (Huron, 2001; McNeil, 1995; Roederer, 1984). This hypothesis predicts that synchronizing movements or vocalizations with other people should not only be experienced as a pleasurable activity, but also increase prosocial commitment and foster subsequent cooperation among the performers. Indeed, in traditional cultures music making and dancing are often collective actions, integrated in important group ceremonies such as initiation rites, weddings, or preparations for battle. This seems to hold for many modern cultures as well: Kirschner and Tomasello (2010) showed that joint music making facilitates prosocial and cooperative behaviors in four-year-old children (Kirschner and Tomasello, 2010). Similar effects have been observed among adults: Anshel and Kipper (1988) found that adult Israeli males score higher on a questionnaire on trust after a group singing lesson in comparison to passive music listening, active poetry reading, or watching a film together (Anshel and Kipper, 1988). Likewise, Wiltermuth and Heath (2009) demonstrated that American students cooperate more after joint singing sessions compared to sessions without singing (Wiltermuth and Heath, 2009).

These wide-ranging prosocial effects of engaging in joint musical activities suggest that our brain may link synchronized actions to a change in social attitude towards the interaction partners. So far, however, the brain areas mediating this linking process remain entirely unknown. In Chapter 4 we provide evidence suggesting that this link may be provided by the brain's reward system, which is known to play a role in our ability to synchronize our actions with an external stimuli (Lewis et al., 2004; Rao et al., 1997; Repp, 2005; Wing, 2002), reinforcement learning (White, 2009) and the modulation of prosocial behavior (Baumgartner et al., 2008;

Delgado, 2008; King-Casas et al., 2005). We suggest that understanding the neural basis of the link between joint musical activity and prosocial behavior may shed light not only on important aspects of human culture but also on the mediators of joint actions.

1.2. Methods and Techniques

Functional MRI (fMRI) is a brain mapping technique developed two decades ago by modifying the structural or classical magnetic resonance imaging (MRI) technique. fMRI detects differences in the magnetic properties of haemoglobin when its configuration changes from the oxygenated to the deoxygenated state (Belliveau et al., 1992; Kwong et al., 1992; Ogawa et al., 1993). Under normal, resting conditions it is assumed that the cerebral blood flow (CBF) and cerebral blood volume (CBV) are regulated by neuronal activity. However, a striking feature of the metabolic responses to functional activation is that rising CBF/CBV uncouples from oxygen consumption (Belliveau et al., 1992). This uncoupling of CBF/CBV and oxygen consumption results in a decrease in deoxyhaemoglobin concentration in the venous pool, providing the blood-oxygen-level dependent (BOLD) contrast used in fMRI studies. By making use of BOLD contrast, fMRI provides an indirect means of assessing neuronal activity.

fMRI has several advantages over other brain imaging techniques. First, it noninvasively records brain signals without the risks associated with radiation exposure inherent in other scanning methods, such as X-ray Computed Tomography (CT) and Positron Emission Tomography (PET) scans. Second, it has high spatial resolution, typically 2–3 mm but resolution can be as good as 1mm. Third, it can record signals from all regions of the brain, unlike Electroencephalography (EEG) and Magnetoencephalography (MEG) which are biased towards recording from the cortical surface.

Although fMRI has been widely used for various fields of neuroscience, studying social interaction as an action related process is relatively challenging, due to the large number of stimulus repetitions required and artifacts resulting from head movements in the scanner. Here, I briefly summarize these two problems, which we encountered, and our efforts to solve them.

First, BOLD changes are typically only one percent above baseline (Ogawa et al., 1990). In order to detect these rather small signal changes it is important to repeat the measurements a large number of times. This necessity for many repetitions of the same stimulus can lead to artificial situations when studying social interactions. In order to overcome this problem, instead of repetitively presenting pictures or videos of social stimuli we asked our participants to interact continuously in real time with social agents (i.e. a game partner, a drummer). Moreover, to motivate our participants we asked our participants to be part of a game during which they could increase their earnings by cooperating with the experimenter.

Another problem that we faced was that, due to the inherent properties of the fMRI equipment, participants had to lie supine on the scanner bed as still as possible while carrying out actions. Even slight head movement may lead to severe reductions in image quality. In addition, upper-arm movements that evoke contractions in the

neck muscles may cause small head movements. Accordingly, we designed tasks involving small movements of the forearm and fingers only. Moreover, we stabilized the upper arms of our participants to avoid head movements yet allow our participants to move comfortably.

1.3. This Thesis

The recently developed line of research devoted to joint action has successfully challenged the traditional ways of studying perception and action in individual minds in isolation. With respect to investigating brains in interaction, a new challenge for social neuroscientists lies in finding ways to explore the neuronal processes underlying true social interactions despite the paradigm limitations imposed by the present brain imaging techniques. Therefore, with the current thesis we not only delineated the brain correlates of joint actions with fMRI, but also explored methods of enabling individuals to interact with other social agents as naturally as possible in the constrained fMRI environment. Hence, we investigated a range of joint actions from playing a simple cooperation game (Experiments 1 and 2) to drumming together (Experiment 3). Although the participants' tasks were experimentally constrained due to the nature of the technique, our experiments always involved real-time interaction with another person in order to keep the interaction as social as possible. These joint action partners varied from an experimenter standing next to the participant (Experiment 1), to a computer (Experiment 2) to drum partners (Experiment 3).

Moreover, we also made advancements in data analysis. In addition to traditional ways of data analysis, we employed an effective connectivity method to test the contribution of the MNS in joint actions in terms of effective connectivity between brain areas (Chapter 3). We did this by employing Granger causality mapping (GCM), which has recently been used to explore the directional information flow between brain areas. This exploratory work of mapping influences between brain areas may suggest a complementary method for neuroimaging studies investigating the neural correlates of joint actions. Therefore, this study not only provides further insight on the neural basis of the joint actions but also a significant methodological advance, that of employing effective connectivity to study social interactions.

In addition, we took the line of research investigating joint action one crucial step further by exploring the continuum from action to social behavior. Recently, interest in the behavioral effects of music making as a collective activity has surged. Many studies have demonstrated a link between joint action in musical context and a change in future social behavior. However, the neural signature of this link is still under-investigated. In the last chapter of this thesis we investigated this link with fMRI by measuring the neural processes associated with synchronized drumming in the reward areas (Experiment 3) and testing the effects of drumming together on social bonding with a prosocial commitment test performed immediately after the Experiment 3 (Chapter 4).

The results presented in this thesis may advance the present knowledge on the neural signature of social interactions, in particular joint actions, in three ways: First, by employing truly interactive paradigms in our first two experiments, we provide one

of the very first direct investigations of the neural basis of joint action, a topic that has previously been restricted to speculative theoretical papers and a few empirical studies (Chapter 2). Second, we shed new light on the contribution of the MNS to joint action by presenting empirical evidence on the information flow within the brain during joint actions (Chapter 3). Finally, we provide the first empirical evidence of both the neural foundation of acting together in a musical context and the subsequent change in prosocial behavior after joint musical activity (Chapter 4). To our knowledge this is not the first study investigating how social synchrony changes future prosocial behavior, but it represents one of the very first studies in which a link between actual prosocial behavior (helping a person pick up dropped pencils) and neural activity in the reward areas is measured. Therefore, it bridges a gap in the fractured literature of the life sciences: behavioural studies of musical behaviour across cultures and the emerging understanding of the neural basis of social reward and affiliation.

Outline of the Thesis

Chapter 1 introduces the concepts, terms and methods used in this thesis.
Chapter 2 presents the first two experiments of this thesis:

Experiment 1 explored the neural mechanisms involved in joint actions when two agents mutually coordinate their actions in real time while playing a cooperation game. For this game we used a custom-made MRI-compatible response box. This box had two arms made of fiberglass sticks resembling the hands of an analog clock, but with the hour hand and minute hands of equal length, was placed on the lower abdomen of the participant lying on the scanner bed. The cooperation game involved two actors: a participant in the scanner and an experimenter standing next to the scanner bed. Participants were able to see the entire response box (via the mirror of the head coil), their own fingers, and the experimenter's fingers. The participant's task was to manipulate his/her stick on the box simultaneously with the experimenter to create a geometrical shape (an angle or a straight line).

In detail, at rest, on the box the experimenter's stick pointed up (12:00 of an analog clock) and the participant's down (06:00). For each game/trial, before the start of actual movements, the experimenter received auditory instructions indicating where (left or right) and when to move her stick. The participant was unaware of these instructions, and received auditory instructions only indicating the final geometrical shape whether to create an angle or a straight line. Accordingly, the experimenter initiated the cooperation game by start pushing the top arm of the clock to the left or right with her index finger according to her instructions. Thereafter the participant pushed his/her stick with the index finger to a direction suitable to achieve the instructed geometrical shape. Actors had 2 seconds to complete the shape and they had to be virtually simultaneous (within 200 ms of each other to convey a mutual feeling of cooperation) while pushing their sticks in order a game/trial to be successful. We introduced this tight time constraint in order to ensure that the participant and experimenter monitors and coordinate the velocity of their movements carefully and continuously throughout the trial as both the spatial and temporal coordination define joint actions. This way, our laboratory paradigm resembled to

real-world joint actions such as lifting a basket together, where the velocity of actions have to be coordinated to avoid tipping over the basket.

In addition to the cooperation games, in the control conditions the participant was asked to (a) passively watch the experimenter moving her stick alone or (b) move his stick alone. With these control conditions we could identify the common voxels for both observation and execution, and thus map the putative MNS in our participants. This revealed that the pMNS involved in both (a) observation and (b) execution included the BA 44, BA 6, IPL and the middle temporal gyrus (MTG). Given that engaging in joint actions requires an integrative processing of two streams of information (visual input and motor output) corresponding to the two agents' actions depending on the task requirements, we mapped the brain areas specifically involved in this integration by comparing the activity during joint actions to the activity during the sum of solo action execution and observation. A network of brain areas showed evidence for this integration during joint actions; we refer to these regions as the integration network. The integration network included the prefrontal, posterior parietal and temporal lobe adjacent to the pMNS: in the frontal lobe the joint action clusters were anterior to those of the pMNS, while in the parietal lobe they were posterior to those of the pMNS. Voxels common to both networks were rare and restricted to the superior parietal lobe and the middle occipital gyrus (MOG). This suggests that, as opposed to previous claims, the integration of observed actions of others with one's own actions is likely to be computed outside of the pMNS in the frontal lobe (Kokal et al., 2009).

Experiment 2 tests whether the activity in the integration network would be as strong as the activity during a task that requires only one-way coordination (one agent adapts his/her behaviors to another). Our experimental task in Experiment 1 was a joint action task, in which two actors had to explicitly take each other's actions into account (mutual coordination). However, we suspected that the motor task this demanded of the participants might have been more complex and difficult in the joint actions conditions (cooperation game) than in the solo conditions (control conditions). For example, in clay pigeon shooting the shooter does not know in advance precisely where and when the clay will go and so has to track the movement of the clay. However, this is clearly not a joint action since the movement of the clay is entirely unaffected by the movement of the shooter. In Experiment 2, we implemented such a task in our paradigm and acquired brain activity while the participants cooperate with a human agent (two-way coordination) or react to the computer to shape the two sticks of the 'clock-like' device in an angle or a straight line (one-way coordination).

This time, movies of a virtual game box replaced the game box of Experiment 1 and were presented to the participants via a data projector on a screen that the participant could view through a mirror. The experimenter stayed in the control room not next to the participant. At the beginning of each game/trial, an index finger holding the edge of the lower stick appeared. After that, the participants controlled that virtual finger using an MR compatible joystick with their right index finger. For the games with the human agent, an index finger holding the edge of the upper stick appeared and the experimenter used her joystick in the control room to control the finger. For the games with the computer, no such finger appeared on the upper stick. For the computer condition, although the participant was led to believe that the

computer controlled the upper stick the experimenter actually controlled the stick, again using her joystick from the control room. The experimenter in the control room was able to view a clone of the movies viewed by the participant. The critical manipulation was that in the human condition, the experimenter viewed both the upper and lower halves of the screen, and could therefore adjust her actions to those of the participant, as in Experiment 1, while in the computer condition; the lower half was occluded, preventing her from reaching to the participants' actions. In the computer condition, the participant therefore had to coordinate his/her actions to those of the 'computer' to reach the target within 200 ms, but the computer (actually the experimenter) did not adjust its movements (one-way coordination).

We extracted brain activity in the peak voxels of the region of interests (ROIs) that we identified in Experiment 1 while participants played with the human agent and reacted to the computer, and then performed comparisons between conditions. Our results revealed that while playing with the human agent brain activity in both the integration network and the pMNS was higher than while playing with the computer. This suggests that, despite the presence of similar biological movement in both conditions (a human experimenter blind to the participant's actions actually played the role of the computer), these brain areas were sensitive to the presence of the mutual coordination that characterizes joint actions (Kokal et al., 2009).

In the previous chapter we concluded that the MNS does not, by itself, directly underlie our ability to integrate our own actions with those of others. In **Chapter 3**, we explored the functional role that premotor sites of the MNS may play in joint actions. By employing Granger causality mapping we demonstrated that the two functionally separate networks (the MNS and the integration network) identified in Chapter 2 were effectively connected. Thus, the MNS may not integrate the actions of the participant with those of the experimenter directly, but rather sends information to a network of regions that do. The MNS could thus play an indirect role by transforming the observed and executed actions into a single code and then sending this information to the brain areas responsible for integration. In addition, we identified predominantly backwards information flow from premotor to posterior regions such as the MOG, primary somatosensory cortex (SI) and the cerebellum. This backward information flow is compatible with forward models proposing that the premotor areas actually send predictions to the sensory areas, and shows that this backward flow can predominate under joint action conditions. This suggests that our brain seems to overcome sensory delays by relying on the predicted actions of others when engaging in joint actions (Kokal and Keysers, 2010).

Chapter 4 presents both an fMRI experiment (Experiment 3) investigating a special form of joint action, namely music making, and a behavioral test (prosocial commitment test) following the scanning sessions.

Every culture has some form of group musical activity. People chant together in churches, dance together in clubs and march together in armies. But why? Unlike sex or food, joint action in a musical context does not provide any obvious fitness advantage, so why is it so universal? To move towards an answer to this question we had people drum together with a drum partner while measuring the participant's brain activity using fMRI. The participants drummed a simple rhythm, in alternating blocks, with two experimenters: one drummed in-synchrony and the other drummed out-of-

synchrony relative to the participants (Experiment 3). After the experiment, we measured the effect of synchronized drumming on 'real-life' prosocial behavior, by 'accidentally' dropping eight pencils in front of the participant and counting the number of pencils the participant picked up to help the experimenter (prosocial commitment test).

We hypothesized that reward areas would be active when individuals are in synchrony with a drum partner (joint drumming), and that these reward signals would facilitate prosocial commitment among drum partners. First, our results revealed that the caudate within the reward system was more active during joint musical activity (synchronous drumming) than asynchronous drumming. Second, in line with previous behavioral studies, participants helped the experimenter who drummed in synchrony with the participants more than the asynchronous one. Importantly, how much they helped was predicted by the amount of activity in the caudate during joint drumming. This demonstrates how the reward system can create a bridge between musical joint activities such as synchronized drumming and prosocial behaviour (Kokal, et al., under review).

Chapter 5 discusses and integrates the main outcomes of this thesis and their implications on further research.

2. Acting Together in and beyond the Mirror Neuron System

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ABSTRACT

Moving a set dinner table often takes two people, and doing so without spilling the glasses requires the close coordination of the two agents' actions. It has been argued that the mirror neuron system may be the key neural locus of such coordination. Instead, here we show that such coordination recruits two separable sets of areas: one that could translate between motor and visual codes and one that could integrate these information to achieve common goals. The former includes regions of the putative mirror neuron system, the latter, regions of the prefrontal, posterior parietal and temporal lobe adjacent to the putative mirror neuron system. Both networks were more active while participants cooperated with a human agent, responding to their actions, compared to a computer that did not, evidencing their social dimension. This finding shows that although the putative mirror neuron system can play a critical role in joint actions by translating both agents' actions into a common code, the flexible remapping of our own actions with those of others required during joint actions seems to be performed outside of the putative mirror neuron system.

2.1. Introduction

Joint actions are "any form of social interaction whereby two or more individuals coordinate their actions in space and time to bring about a change in the environment" (Sebanz et al., 2006a).

As very few studies have investigated brain activity during joint actions (Newman-Norlund et al., 2008; Newman-Norlund et al., 2007a; Sebanz et al., 2006b; Sebanz et al., 2007) the brain mechanisms supporting joint actions are still unknown. In comparison, there are more studies investigating brain activity while participants executed an action or/and observed an action. In the monkey, single cell recordings showed that some neurons, called mirror neurons, were active both during the observation and execution of similar actions (Fijii et al., 2007; Fogassi et al., 2005; Gallese et al., 1996; Keysers et al., 2003; Kohler et al., 2002; Umilta et al., 2001). In humans, voxels in similar locations have been found to be active during action observation and execution and form what should be called the *putative* mirror neuron system (Gazzola et al., 2006; Gazzola and Keysers, 2008; Gazzola et al., 2007a; Gazzola et al., 2007b; Grafton et al., 1996; Hamilton et al., 2007; Iacoboni and Dapretto, 2006; Keysers and Gazzola, 2006; Rizzolatti and Craighero, 2004; Rizzolatti et al., 1996). The term 'putative' here underlines the fact that if a voxel in an fMRI experiment shows an increase in BOLD both during action observation and

execution, this suggests that it could contain mirror neurons, but it could also contain distinct but interdigitated populations of neurons involved in action observation only and execution only, commending caution in interpretation (Gazzola and Keysers, 2009). The monkey mirror neuron system and its putative human equivalent have been implicated in many aspects of social interactions, including imitation (Iacoboni et al., 1999), empathy and simulation (Fijii et al., 2007; Fogassi et al., 2005; Gallese et al., 1996; Gazzola et al., 2006; Gazzola and Keysers, 2008; Gazzola et al., 2007a; Gazzola et al., 2007b; Keysers et al., 2003; Kohler et al., 2002; Umilta et al., 2001) , mind-reading (Gallese, 2003; Gallese and Goldman, 1998) and language (Rizzolatti and Arbib, 1998).

Recently, the putative mirror neuron system was proposed to play a central role in joint actions because of the close link between perception and action provided by these brain regions (Knoblich and Jordan, 2002; Newman-Norlund et al., 2008; Newman-Norlund et al., 2007a). According to this proposal, actors use simulation to predict the intentions and consequences of the actions of their co-actor. This would help the actor adjust his own action plans to the predicted actions of co-actor in order to successfully achieve a joint goal. Going one step further, Newman-Norlund and coworkers (2008), in a virtual lifting task, found that the BOLD signal in the right inferior frontal gyrus (IFG) was larger while participants balanced a ball together with another agent (joint action) compared to when they balanced the ball alone. The authors suggest that this finding indicates a direct role of the putative mirror neuron system in the integration of observed and executed actions during joint actions. However much of the IFG does not have mirror properties, and given the authors have not mapped the putative mirror neuron system of their participants, the IFG but not the putative mirror neuron system may be responsible for this effect (Thioux et al., 2008).

Here we propose that a typical joint action requires at least three, more or less intertwine but conceptually separable processes: observing the actions of others (*observation*), executing one's own actions (*execution*) and integrating *obs* and *exe* to tune one's own actions to those of others (*integration*).

In contrast to the interpretation of Newman-Norlund and coworkers (2008), we hypothesize that the putative mirror neuron system does not participate in the integration component of joint actions. This is because the neurons in the monkey's premotor cortex that have been described to respond to the sight of other people's actions show a *fixed* relationship between effective observed and executed actions (Gallese et al., 1996). For both strictly and broadly congruent mirror neurons, this relationship is one of *correspondance*, with 'correspondance' meaning that the actions have the same goal (broadly congruent, 60.9%) or the same goals and means (strictly congruent, 31.5%). For the minority (7.6%) of 'non-congruent' or 'logically related' visuo-motor neurons this relationship is different, and can include complementarity (e.g. execution of grasping and observation of placing), but again, this relationship is fixed over trials. By fixed relationship, we do not preclude the fact that extensive training can change this relationship (Catmur et al., 2007), but that it is not known to change in seconds based on task demands. The putative mirror neuron system could therefore promote joint actions by constantly linking the observation of actions to the motor programs for *similar* or complementary actions (Iacoboni et al., 1999; Rizzolatti and Craighero, 2004), but the integration needed in joint actions *has* to be

more flexible: during joint actions, unlike imitation, the task determines the nature of this integration, which can vary from doing the same (e.g. lifting a table together) to the opposite of a partner (e.g. moving a table with one partner moving forwards and one backwards) in seconds. This rapid task-dependent redefinition of the visuo-motor integration goes beyond the known properties of mirror neurons and logically related visuo-motor neurons and is likely to recruit separate brain regions.

Testing this hypothesis therefore necessitates (i) a joint action task with trials requiring doing a similar action and trials requiring doing the opposite of a partner to achieve a common goal and (ii) observation *(obs)* and execution *(exe)* control tasks to map the putative mirror neuron system in the same participants. In *Experiment I* we therefore introduced a novel joint action paradigm (Fig. 1A and Methods and Materials) that encompasses conditions in which participants only observe or only execute solo actions as well as joint action conditions in which they additionally have to integrate observation and execution by executing an action similar or opposite to the one observed. We identified regions involved in *integration* during joint actions by requiring that activity in joint actions exceeds that during solo observation plus execution (if *integration*>0 then *joint action* (=*obs*+*exe*+*integration*)>*obs*+*exe*). This requirement is similar to the criterion of superadditivity used to identify regions involved in multisensory integration (Beauchamp, 2005), and we will therefore abbreviate regions showing evidence for superadditive integration during joint actions as 'sJA'. It also resembles the definition of imitation selective areas introduced by (Iacoboni et al., 1999): imitation>exe+obs. The location of this network involved in *integration* can then be compared with that of the network of the putative mirror neuron system defined as voxels active during observation and execution. Finding none or minimal overlap between the networks would support our hypothesis that the putative mirror neuron system is not the primary locus of the *integration* process in joint actions. In contrast, finding that the sJA network falls within the putative mirror neuron system, particularly in the IFG, would support Newman-Norlund and coworkers (2008) interpretation that the *integration* is computed within the putative mirror neuron system network.

Furthermore, joint actions in the strict sense require *mutual* coordination between two agents. While shooting clay pigeons for instance, we need to adapt our own actions to the movements of an object in the outside world, which is an example of one-way coordination of an agent to an event in the outside world. This, however, does not qualify as a joint action because clay-pigeons do not react to our movements. In contrast, lifting a table together *does* qualify, because the lifters *mutually* coordinate their movements to one another's. To examine whether brain regions identified in *Experiment I* are sensitive to this distinction, in *Experiment II* we scanned half of the participants a second time, while playing the same cooperation game (a) with another person that adapts her movement to those of the player (mutual coordination, true joint actions) or (b) with a computer that does not (one-way coordination).

2.2 Materials and Methods

2.2.1 Experiment I

Participants: 18 healthy volunteers (all right-handed; 10 female and 8 male; mean age 23.7 years ranging 20-45 years) with normal or corrected to normal vision and without a history of neurological, major medical, or psychiatric disorders. The experiment was approved by the Medical Ethical Commission of the University Medical Center Groningen, the Netherlands. Participants gave informed consent and were paid for their participation.

Response Box: We used a custom-made MRI-compatible response box. The box was placed on the lower abdomen of the participant who was lying on the scanner bed (Fig. S1A). Using the mirror of the head coil participants were able to see the entire response box, their own fingers as well as the fingers of the experimenter who was standing next to the scanner bed. The participant and the experimenter wore MRI-compatible headphones for auditory instructions. The response box had 2 individual arms made of fiberglass sticks resembling the hands of an analog clock with an hour hand and a minute hand of equal length (11 cm, Fig. S1B). At rest, the experimenter's stick pointed up (12:00 of an analog clock) and the participant's down (06:00). Four sensors ('S1'-'S4' in Fig. S1B) placed at 2, 4, 8 and 10 o'clock, measured the time point at which the experimenter or participant reached the target position with their stick by pushing the stick with their index finger. The spring-loaded sticks returned to the initial positions (12 and 6 o'clock) when released at the end of the trial. Two starting buttons ('SB1' and 'SB2' in Fig. S1B) at locations 12 and 6 o'clock served as 'home base' for the experimenter and participant respectively (Fig. S1B), and red LEDs ('RL' in Fig. S1B) were turned on for as long as the experimenter or participant pressed her or his starting button.

Procedure: In the fMRI session, the experimenter and the participant (both right-handed) played a cooperation game or performed one of three non-cooperative control conditions while the participant was being scanned.

The task of the participant in the joint action conditions was to cooperate with the experimenter to shape the two sticks of the box in either an angle or a straight line (see Fig. S1C, D and Video S1). At the beginning of each trial, both players had their index finger on their starting button (SB1 and SB2 in Fig. S1B). Before the actual movement, the experimenter received auditory instructions indicating where (left or right) and when to move her stick. The participant was unaware of these instructions, and received auditory instructions only indicating whether to create an angle (*ang)* or a straight line (*str*, Fig. S2). The experimenter, present in the scanner room, initiated the cooperation by moving the top arm of the clock to the left or right. The participant had to react by starting to move the lower arm of the clock in the direction suitable to achieve the target shape (Video S1). More specifically, the participant had to release his start button after the experimenter had left hers, which occurred between 1 and 2s (random interval) after the participant had received the angle or straight instruction. Thus, s/he had to carefully watch the experimenter's actions to determine (a) *when* the experimenter started her movement and (b) *which side* the experimenter moved towards. This allowed the participant to determine when to start his/her own action

and, in combination with the knowledge of the target shape (straight or angle), which side to move his/her stick towards. The experimenter and participant then had to reach the target location virtually simultaneously (within 200 ms of each other) to jointly win the trial. This tight time constraint ensured that the participant and experimenter had to monitor and coordinate the velocity of their movements carefully and continuously throughout the trial, requiring both the spatial and temporal coordination that defines joint actions. It also makes our laboratory paradigm similar to real-world joint actions such as lifting a dinner table, where the velocity of actions have to be coordinated to avoid tipping over the objects. The experimenter varied her initial movement velocity from trial-to-trial and participants responded to these changes showing that they indeed adjusted their own actions continuously to those of the experimenter (see Video S1). Thereafter, both agents had to, and did, adjust their movements to the velocity of the other to meet the common goal of reaching the target location within 200 ms of each other, conveying a mutual feeling of cooperation.

After the end of a trial, both players had to place their index finger back onto their respective starting button. At the end of each run, the participant and experimenter were informed about how many points they have jointly earned to maintain motivation. At the end of the experiment, we debriefed the participants about the experiment. We asked the following questions: Did you perceive the trials as games? Did you try to cooperate with the experimenter? Was she cooperating with you? Which game did you find harder; angle or straight? At debriefing, all participants reported perceiving the task as a cooperation game, trying to be as successful as possible and feeling that the experimenter adjusted her movement to match theirs and vice versa. None of the participants made more than 3 errors out of the 72 game trials played per run. Unfortunately, reaction time data is not available because for 10/18 participants, one of the two target locations were hard to reach within the space constraints of the scanner, and they were instructed that the direction and timing of the movement was more critical than reaching the actual target location. For these participants, during scanning, the experimenter kept track of the number of direction errors (i.e. not going towards the experimenter's side in angle or going to the experimenter's side in straight trials), and verbally informed the participants of their performance. Inspection of the data from these 10/18 participants however did not suggest any systematic differences with those of the remaining 8 participants.

The experiment contained 6 conditions that were arranged in blocks of 8 trials lasting between 45 and 54 s (depending on the random intervals separating trials, Fig. S2).

1) *Angle (ang)*: 8 trials separated by 2.3 s all starting with the instruction 'angle' (450 ms with a 150 ms silence added at the end to match the length of 'straight' sound).
2) *Straight (str)*: as in *ang*, but all trials started with the instruction 'straight' (600 ms).
3) *Mixed (mix)*: 4 angle trials randomly intermixed with 4 straight trials.Blocks of type 1-3 involve joint actions and 1.75 s before each block a 130 ms tone (sine wave, 440 Hz) instructed participants that they would have to play the cooperation game. In each block, the experimenter moved her stick 4 times to the right and 4 times to the left, in random order.

4) *Sound (snd)*: participants heard the 'angle' and 'straight' instructions using the exact same timing as in a *mix* block. 1.75 s before the onset of a *snd* block, participants heard a verbal instruction 'eyes close' (900 ms) ordering them to close their eyes and indicating that the next block required them to listen to the auditory instructions without further actions. 1500 ms after the end of *snd* blocks, a voice stating 'eyes open' (900 ms) instructed participants to reopen their eyes.
5) *Observation (obs)*: participants only viewed the experimenter move her stick to the right or left using the exact same timing as in a joint action block. 1.75 s before the block, the verbal instruction 'look' (400 ms) instructed the participants only to observe the experimenter.
6) *Execution (exe)*: In conditions 1,2,3 and 5, a red light (RL in Fig. S1B) was turned on whenever the experimenter placed her finger on the start button (SB in Fig. S1B) and turned off whenever she left the SB to start her action. In the execution condition, the experimenter's RL was turned on and off with the same timing as in the conditions 1,2,3 and 5 without the experimenter being visible. The participant had to move his/her stick to the right or left whenever he/she saw the red light turn off on the box, ensuring that the timing of the participant's actions was the same as in the joint action blocks but not triggered by a biological action. The participant could choose what side to go to, but was instructed by the experimenter to avoid going to the same side constantly. A verbal instruction 'action' (400 ms) presented 1.75 s before the block indicated the nature of the block.

Blocks were separated by 14 ± 2 s random pauses (including the verbal instruction or sound indicating the type of block to follow). Each run lasted 720 s and contained 2 blocks of each of the 6 conditions and a feedback at the end. Five runs were acquired, for a total of 10 blocks of each condition. The order of the conditions was counterbalanced between runs and participants. Stimuli were programmed and presented using the Presentation software (Neurobehavioral systems, Davis, CA).

Participants were familiarized with all the conditions during a training session performed outside of the scanner on a separate day. This training was composed of three 720 s sessions identical to those used in the main experiment. In the third of these sessions, all participants performance was perfect (i.e. not a single error in the 72 trials). None of the participants reported being confused about the conditions during the main experiment in the scanner. This training session also ensured that those participants that were unable to reach the sensors in the fMRI experiment were familiar with the time constraints of the game, which were accurately measured out of the scanner, but impossible to measure during scanning for these participants.

Data acquisition: Imaging was performed with a Philips Intera 3T Quaser with a synergy SENSE head coil and maximum gradient strength of 30 mT/m. Head movements were minimized by using foam padding and never exceeded 3mm in a run. We used a standard single shot EPI with TE = 28 ms, TA= 1.25 s, TR= 1.3 s, 28 axial slices of 4 mm thickness, without slice gap and a 3.5x 3.5 mm in plane resolution acquired to cover the entire brain. The first five volumes of each functional run were discarded for the longitudinal magnetization to approach equilibrium. A T1 weighted structural scan was acquired with TR=15.31 ms, TE=3.6 ms, flip angle=8 deg.

Data preprocessing: Using SPM2 (www.fil.ion.ucl.ac.uk/spm) implemented in MATLAB 6.5 (Mathworks Inc., Sherborn, MA, USA). All EPI volumes were aligned to the first volume acquired for each participant and a mean EPI image generated after realignment. Spatial normalization was performed by co-registering the structural volume to the mean EPI, segmenting the coregistered structural image, determining the normalization parameters required to warp the gray matter segment onto the gray matter MNI template, and applying these parameters to all EPI and structural volumes. The normalized EPI images were smoothed with a 6 mm FWHH isotropic Gaussian kernel.

General data analyses: Functional data were analyzed using a general linear model (GLM) separately for each participant and voxel using SPM2. Although the experiment was presented as a block design, we modeled the data in a event related fashion because examination of the signal time course within the blocks showed clearly visible peaks for each trial.

Single participant analyses: the GLM was performed using separate auditory predictors for the conditions *ang*, *str*, *mix* and *snd* to capture brain activity caused by hearing the words "angle" or "straight" and separate action predictor for the *ang*, *str*, *mix*, *obs* and *exe* conditions to capture brain activity triggered by executing and/or observing the finger movements. Each predictor was a boxcar function that reflected the trial-by-trial timing of the auditory and movement epoch of the condition (much as in Fig. S2, but the action predictor corresponded to the union of the experimenter's and participant's action time course). The boxcar functions were convolved with the haemodynamic response function, and fitted separately for each run to the data. In addition, the head motion and rotation along the three axes were entered as 6 covariates of no interest in the design matrix to single out motion artifacts although motion never exceeded 3mm within a run. Given that little time separated the auditory instructions from the actions within a block (average=1500 ms), the auditory and action predictors overlap in time (after convolution with the hrf), and the attribution of a brain activity to one rather than the other uncertain. Instead of analyzing the parameter estimates for the auditory and action predictor separately, we therefore combined them by summing the surface under the fitted auditory and action predictors. This was done simply by multiplying the parameter estimates (Beta) obtained from the GLM with the surface (S) under their respective predictor ($S=Beta_{auditory}xS_{auditory} + Beta_{action}xS_{action}$). Brain activity across conditions can then be compared using this surface. For instance whether for a particular voxel, the activity in the *str* condition exceeds that of the sum of the *snd*, *exe* and *obs* condition, a contrast value $C= (Beta_{auditory}xS_{auditory} + Beta_{action}xS_{action})_{str}-(Beta_{auditory}xS_{auditory} + Beta_{action}xS_{action})_{snd}- (Beta_{action}xS_{action})_{obs}-(Beta_{action}xS_{action})_{exe}$ can be calculated and tested using the null hypothesis C=0. Note that $S_{auditory}$ and S_{action} are relatively constant across participants and conditions ($angS_{auditory}$ average=16, s.e.m.=0.0002 and $angS_{action}$ average=40.06, s.e.m=0.86, $strS_{auditory}$ average=16, s.e.m.=0.0029 and $strS_{action}$ average=40.14, s.e.m=0.88, in arbitrary units) because the timing of the conditions was relatively constant.

Population analyses: At the second level of analysis, to implement a random effect analysis, contrast estimates obtained separately for each participant were tested at the population level, using one-sample t-tests or analyses of variances (ANOVA)

that test whether the average contrast differs from zero. Only results that are significant both at $p < 0.001$ uncorrected and $p < 0.05$ corrected using false discovery rate are reported as significant. Only clusters of at least 10 voxels are shown.

pMNS (Putative Mirror Neuron System) definition: In particular, to determine voxels involved in the putative mirror neuron system, the surface under the curve in *obs* was compared against zero (t-test), and the same was done for *exe*, and only those voxels with significant results in both analyses at the second level were considered to belong to the putative mirror neuron system (i.e. $(Beta_{action}xS_{action})_{obs}>0$ & $(Beta_{action}xS_{action})_{exe}>0$, where & is a logical, both at $p_{unc}<0.001$ and $p_{fdr}<0.05$) and; here, using the surface under the curve or the parameter estimate alone is mathematically virtually equivalent because S_{action} was very similar across participants). This operational definition is far from perfect: a voxel can be involved in both execution and observation although the individual neurons within that voxel are not involved in both, which is why we refer to these voxels, not as 'mirror', but as *putatively* mirror. This definition is however relatively well established in the neuroimaging literature (Chong et al., 2008; Gazzola et al., 2006; Gazzola et al., 2007a; Gazzola et al., 2007b) and is the most direct translation of the original definition at the single cell level in monkeys (Gallese et al., 1996; Keysers et al., 2003; Kohler et al., 2002; Umilta et al., 2001). A similar definition is also used in domains of emotions (Jabbi et al., 2007; Singer et al., 2004; Singer et al., 2006; Wicker et al., 2003) and sensations (Blakemore et al., 2005; Keysers and Perrett, 2004; Keysers et al., 2004). Given that the main point of the present paper is that joint actions require more than the putative mirror neuron system alone, showing this while running the risk of *over*estimating the extent of the putative mirror neuron system (e.g. by including voxels that contain intermixed populations of responding to only the observation or only the execution of actions or responding to less general factors such as attention) actually strengthens the point.

sJA (Superadditive Voxels in Joint Actions) definition: to map regions showing activity that indicates their contribution in integrating observed and executed actions, two contrasts were calculated at the first level ($C_{ang}= (Beta_{auditory}xS_{auditory} + Beta_{action}xS_{action})_{ang}-(Beta_{auditory}xS_{auditory} + Beta_{action}xS_{action})_{snd}- (Beta_{action}xS_{action})_{obs}-(Beta_{action}xS_{action})_{exe}$ and $C_{str}=(Beta_{auditory}xS_{auditory} + Beta_{action}xS_{action})_{str}-(Beta_{auditory}xS_{auditory} + Beta_{action}xS_{action})_{snd}- (Beta_{action}xS_{action})_{obs}-(Beta_{action}xS_{action})_{exe}$). This definition included the *obs* and *exe* conditions as outlined in the introduction plus the *snd* condition to control for the effects of the auditory instructions given during the joint action tasks. Again, the logic of this definition is that what distinguishes joint actions from solo actions is that joint actions not only include the processes of observing actions and executing actions, but also additionally requires partners to *integrate* these two processes to achieve a goal. This integration is what the sJA maps try to capture. They do so by deducing that if *joint action= obs + exe + integration* (+*snd*), and *integration*>0, then *joint action-obs-exe-snd=integration* and has to be >0. Note that since the baseline condition between trials and blocks included the vision of the game box, the parameter estimates for the various conditions should capture deviations from this baseline, namely the sight of the experimenter's finger action in obs, and the motor control and observation of the participant's own finger movement in the exe condition. Subtracting both *obs* and *exe* from joint actions therefore does

not represent a double subtraction of the visual input, but two separate subtractions of the unique visual components. The 18 C_{ang} and the 18 C_{str} contrasts (one per participant) were entered in a one way ANOVA without constant, and the global null conjunction calculated to estimate the likelihood of the null hypothesis (m(C_{ang})<=0 & m(C_{str})<=0) that the voxel was not involved in either joint action (Friston et al., 2005). A global null hypothesis is appropriate here because unlike the definition of the putative mirror neuron system requiring that both *exe* and *obs* be above zero, for a voxel to be involved in joint actions it is sufficient that it be involved in one of the two joint actions.

Examining the parameter estimates in the resulting SPM showed however that sJA contained voxels in which the activity in *ang* or *str* was above *exe*+*obs*+*snd* without being above the activity in *exe*, *obs* and *snd* taken individually. This was the case for instance when *obs* and *snd* had negative parameter estimates, because *exe*+*obs*+*snd* was then less than *exe* alone. To prevent this unwanted effect, we additionally required that sJA voxels fall within an inclusive mask where ((*ang*>*exe* and *ang*>*obs* and *ang*>*snd*) or (*str*>*exe* and *str*>*obs* and *str*>*snd*)), with each individual contrast in that logical conjunction taken at p<0.05 uncorrected.

sJA' (Alternative sJA) Definition: To examine whether reductions in BOLD during *snd* only could have artificially inflated the number of sJA, we also examined which voxels satisfy a criterion excluding *snd* (i.e. the contrast *joint action*-(*exe*+o*bs*) instead of *joint action* -(*exe*+*obs*+*snd*), see Fig. S3A).

maxJA (Joint Action Voxels Calculated Using a Maximum Requirement) Definition: As an alternative to the sJA definition that rests on a criterion of superadditivity, we explored the impact of using what has been called a "maximum requirement" as well (Beauchamp, 2005). This requirement typically states that multisensory response have to be larger than the maximum of the unisensory responses (Beauchamp, 2005). Adapted to our situation we therefore require that joint action related activity be more than the maximum activity in *observation* and *execution* of solo actions (*ang*> max (*exe*,*obs*) *or str*> max (*exe*,*obs*). In order to do so, for each participant we calculated two contrast maps using ImCalc in SPM: *ang*-max (*exe*,*obs*) and *str*-max(*exe*,*obs*). Second, we created a second level ANOVA that included these two contrast maps for each participant. Third, we performed a global null conjunction between the *ang*-max (*exe*,*obs*) and *str*-max (*exe*,*obs*). This map was then thresheld at p<0.001 uncorrected (which survived also to p<0.05 fdr correction). Results reflect those voxels in which either the *ang* or the s*t*r condtion (or both) exceeded the maximum of *exe* and *obs*.

Analysis of the peak voxels: To compare the functional properties of the putative mirror neuron system and sJA regions, we selected the location of the peak *obs* activations in the main putative mirror neuron system clusters (dorsal and ventral premotor and parietal clusters and MTG) and identified locations of peak activity according to the global null conjunction in the sJA that were in anatomically similar locations (dorsal and ventral frontal and parietal, precuneus and high-level visual cortex). Peaks were extracted both from the left and right hemisphere in corresponding locations but the pattern in the right hemisphere was so similar to that in the left hemisphere, that only those of the left hemisphere are shown in Figure 1C. We then extracted the mean signal time course in these peak voxels and analyzed this

signal using a GLM with the same predictors used for the voxel-by-voxel analysis but using MarsBar (http://marsbar.sourceforge.net). The surface estimates of the conditions as defined above together with the MNI coordinates of the peaks was then plotted in the Figure 1C. Thereafter, a number of planned comparisons were performed at the second level based on the surface estimates of the 18 participants. In particular, for sJA peak voxels, we tested whether the activity in *exe*, *obs, ang, str* exceeded zero (one-tailed t-test using a threshold of 0.01/6 to correct for the fact that the test was performed in 6 peak voxels) to check whether the ROIs behave as would be expected for the putative mirror neuron system and whether the joint action conditions show activity above baseline. Additionally we tested in sJA peak voxels whether the activity in *ang* and *str* exceed the sum of *exe* + *obs* (contrast *ang* > *exe+obs* and *str*> *exe+obs*, one-tailed t-test) to examine whether the voxels designated to joint action showed greater activation during joint actions than the sum of *exe* + *obs* independent of deactivations during *snd* condition (triangles in Fig. 1C). For putative mirror neuron system peak voxels, we tested whether the parameter estimates in the *ang* and *str* condition exceeded zero to check whether the putative mirror neuron system is involved in joint actions (the result was always significant) and whether the activity in the *ang* condition and the *str* conditions exceeded the sum of *exe*, *obs* and *snd* (contrast *ang- exe-obs-snd* and *str-exe-obs-snd*, results were never significant) using one-tailed t-test with a threshold of 0.01/5 to correct for 5 peak locations in all 4 tests. Finally, in all 11 peak voxels we examined the effect of rule switching by examining if the mixed condition exceed the unmixed joint actions conditions (contrast *2mix>ang+str*, one tailed t-test against zero, threshold 0.01/11) and we compared *ang* and *str* conditions (*ang-str*, two-tailed t-test) (Fig. S4B).

Results were not boneferoni corrected for the number of comparisons (8 for sJA and 6 for putative mirror neuron system) because they were planned a priori. We also extracted the mean activity from the entire clusters of subthreshold voxels in both the putative mirror neuron system and the sJA, but results were virtually identical to those of the peaks, showing that the peaks were indeed representative of the activity in clusters, and we therefore only report the results of the peak analyses.

2.2.2 Experiment II

The general procedures were very similar in *Experiment I* and *II*. In the interest of space, we will restrict ourselves to the differences between the methods below.

Participants: 8 healthy volunteers (all right-handed; 5 female and 3 male; mean age 23.5 years ranging 21-24 years) from *Experiment I*.

Stimuli: Movies of a virtual game box replace the game box of *Experiment I*. The pictures of the custom-made MRI-compatible response box that we used for the first experiment were presented to the participants via a data projector on a screen that the participant could view through a mirror. Stimuli were programmed and presented using Presentation software (Neurobehavioral systems, Davis, Ca.)

At the beginning of each trial, an index finger holding the edge of the lower stick appeared. After that, the participants controlled that virtual finger using an MR compatible joystick (fORP, Current Designs, Inc., Philadelphia, USA) with their right index finger. For the 'human agent conditions' an index finger holding the edge of the

upper stick appeared and the experimenter used her joystick in the control room to control the finger (Fig. S1E, G). In the computer condition, no such finger appeared on the upper stick (Fig. S1F, H). Although the participant was lead to believe that the computer controlled the upper stick in the computer condition, the experimenter actually controlled the stick, again using her joystick from the control room. The experimenter in the control room viewed a clone of the movies viewed by the participant. The critical manipulation was that in the human condition, the experimenter viewed both the upper and lower half of that screen, and could therefore adjust her actions to those of the participant, as in *Experiment I*, while in the computer condition, the lower half was occluded, preventing her from reaching to the participants actions. In the computer condition, the participant therefore had to coordinate his/her actions to those of the 'computer' to reach the target within 200ms, but the experimenter did not adjust hers (one-way coordination), whilst in the human condition, the two agents mutually adapted their actions to each other, creating the social loop so characteristic of joint actions (mutual coordination). What differs is whether the experimenter coordinated her actions with those of the participant (mutual vs. one-way coordination). After the end of each trial, both players had to place their joystick back onto the middle position. At rest, participants saw the entire response box with the experimenter's stick pointed up (12:00 of an analog clock) and the participant's down (06:00).

Procedure: All participants were invited to participate in *Experiment II*, but only 8 accepted. Only the joint action conditions (angle and straight) were acquired, but while the participant played with a human agent and what he/she thought to be a computer. The timing of conditions was as in *Experiment I*. The actual task was as in *Experiment I*: to cooperate with a human agent or react to the computer to shape the two sticks of the response box in an angle or a straight line (see Fig. S1E-H). The experimenter and participant then had to reach the target location virtually simultaneously (within 200 ms of each other) to jointly win the trial. The experimenter varied her initial movement velocity from trial-to-trial in both the human and computer condition. In the human condition, both agents then adjust their movements to the velocity of the other to meet their common goal, conveying a mutual feeling of cooperation. In the computer condition, the burden of the adjustment rested entirely with the participant, as the experimenter was blind to the movements of the participant (one-way coordination). At the end of the experiment, we debriefed the participants about the experiment. We asked the following questions: Did you perceive the trials as games? Did you try to cooperate during the experiment? Was there a difference between human and computer? Which game did you find harder; angle or straight? Were you able to control the joystick? Participants indeed perceived the computer condition as more difficult, but performance did not differ significantly (human 69% correct; computer 73.5% correct, t-test, $p>0.14$) demonstrating that the participants successfully dealt with the challenge. The experimenter took care during the computer condition to generate movements that were similar in complexity and total duration to those in the human condition, including decelerations and accelerations to simulate those that occurred in response to the participant's behaviour in the human condition. The lack of significant differences in total movement duration for the experimenter in the two conditions (see Results) confirms the similarity of overall movement

characteristics. What changes however, was that these movements were no longer contingent with those of the participant, and participants reported perceiving the difference between human and computer agents in *Experiment II* (e.g. "the computer never waited for me!", one of the participants declared).

Participants were familiarized with the experimental conditions and the joystick during a short training session performed outside of the scanner prior to the scanning. In this session, participants were introduced to the computer condition by showing them a prerecorded motion (computer moving the stick), which they would observe and engage in joint actions with it. This was in contrast to the human condition in which they could see the experimenter side-by-side with them, playing a number of joint action trials to reinforce the feeling of cooperation. Moreover, joystick calibration and training with an online feedback was performed in the scanner before the start of the experiment. All participants reported that they perceived the computer conditions as controlled by a computer whilst they truly felt that they were playing with the experimenter in the human agent conditions.

Data acquisition & Preprocessing: as in *Experiment I*.

General data analyses: Functional data were analyzed using a general linear model (GLM) separately for each participant but only for the peak voxel of the ROIs determined in *Experiment I* and specified in Fig. 1. This was done because 8 participants provide sufficient statistical power while controlling for family wise error in a small number of ROIs but not for a whole brain analysis. Examining the responses from all the trials in each block using the surface analysis of *Experiment I* revealed a significant main effect of agent in a 2 Agent x 12 ROIs repeated measurement ANOVA ($p<0.04$, human>computer), but examining the time course of the responses aligned to the beginning of each block revealed that in all ROIs, the responses decreased over the 8 trials of the blocks. We therefore remodeled the data using two sets of predictors for each block: one for the first and one for the remaining 7 trials. This analysis is the one we present in the manuscript. Signals were then analyzed using the same procedure as in *Experiment I* (see section "Analysis of peak voxels"), but using a repeated measurement ANOVA with 12 ROIs, 2 Agents (human vs computer) and 2 conditions (angle vs. straight). The absence of a main effect or interaction of condition (all $p>0.18$) motivated us to sum activity in the two conditions (angle and straight) and use a 2 Agent x 12 ROI ANOVA instead to test the one tailed prediction that areas recruited during joint actions should respond more to the human agent than the computer. Using the first event only slightly improved the significance of the main effect of agent (from $p<0.04$ with all trials to $p<0.013$ with the first trial only, ANOVA 12 ROIs x 2 Agents). Least Significant Difference post-hoc t-tests were used to test differences in individual ROIs using a cut-off of $p<0.05$.

2.3 Results

2.3.1 Experiment I

To examine the role played by the putative mirror neuron system in joint actions, we first localized the putative mirror neuron system (Gazzola et al., 2007b; Keysers and Gazzola, 2006) by inclusively masking the contrast *obs*-rest with *exe*-rest

(Fig. 1B in blue and see Table S1). This revealed areas corresponding to those reported in the literature including premotor (BA6, BA44), parietal (SI, SII, PF, SPL) and high level visual areas (Fijii et al., 2007; Fogassi et al., 2005; Gallese et al., 1996; Gallese et al., 2004; Gazzola et al., 2006; Gazzola et al., 2007a; Gazzola et al., 2007b; Grafton et al., 1996; Hamilton et al., 2007; Heyes, 2001; Iacoboni and Dapretto, 2006; Iacoboni et al., 1999; Keysers and Gazzola, 2006; Keysers et al., 2003; Keysers and Perrett, 2004; Kohler et al., 2002; Newman-Norlund et al., 2007b; Rizzolatti and Craighero, 2004; Rizzolatti et al., 1996; Umilta et al., 2001) (see Table S6 for a list of abbreviations). We then mapped brain areas involved in the dynamic integration of action observation, execution and task requirements by searching for voxels in which brain activity during joint actions (*str* or *ang*) exceeds the sum of that during *exe*, *obs* and *snd.* Voxels satisfying this criterion will be referred to as superadditive voxels in joint actions or *s*JA voxels and Figure 1B (green) and Table S2 show their location. A central finding of this analysis is that sJA voxels do not consistently fall within the putative mirror neuron system but are adjacent to it. In the frontal lobe, sJA clusters were anterior to those of the putative mirror neuron system while in the parietal lobe, the sJA clusters were posterior to those of the putative mirror neuron system. Indeed, voxels common to both networks were rare and restricted to the superior parietal lobe and higher-level visual areas (Fig. 1B in red and see Table S3). Examination of the parameter estimates (Fig. 1C) of putative mirror neuron system and sJA peak locations shows that although the pattern of activity is somewhat similar, a functional dissociation exists: in putative mirror neuron system peak locations *str* and *ang* activity does not exceed *obs*+*exe*+*snd*, and the putative mirror neuron system therefore does not show evidence of *additional* processes during the integration of *obs, exe* and *snd* during joint actions. In sJA peak locations on the other hand, the activity is never significant during both *exe* and *obs,* showing that these areas are not part of the putative mirror neuron system. This does not mean however that the putative mirror neuron system is not involved in joint actions given that the putative mirror neuron system regions were significantly activated during *ang*, *str* as well as *obs* and *exe*, but that the putative mirror neuron system was not involved in the additional integration process.

Given that in most sJA regions, the *snd* condition determines a reduction of BOLD compared to baseline, we examined the voxels satisfying a definition of sJA excluding *snd* (i.e. *joint action*> *exe*+*obs*; see Fig. S3, Table S6 and triangles in Fig. 1C). This revised definition (sJA') leads to very similar findings in frontal and parietal but not in the occipito-temporal region (around p11 in Fig. 1B) where listening to auditory instructions with closed eyes (*snd*) may have drawn attentional resources away from visual areas, and artificially inflated the contrast of joint actions against the control conditions. The overlap between sJA' and putative mirror neuron system is however not larger than that between sJA and putative mirror neuron system. These control analyses strengthen the findings in frontal and parietal sJA, but commands care in interpreting the function of occipito-temporal sJA.

Finally, it has been argued that brain regions can be involved in integrating two modalities without the response to the multimodal stimulus exceeding the sum of its unimodal components (Beauchamp, 2005). An alternative, and sometimes more sensitive criterion, may be to request that the response to the multimodal stimulus

exceeds the highest of its unimodal components (Beauchamp, 2005). Applying this maximum requirement to our data (see Materials and Methods and Fig. S5) however lead to results that differed very little from those of the previous analyses: none of the frontal, and only small regions of the parietal and temporal putative mirror neuron system clusters showed overlap with the voxels showing evidence for integration during joint actions. Indeed, in our particular data set, this maximum criterion was more conservative than the superadditivity criterion. Examining the parameter estimates of Figure 1 help understand why: in many sJA regions, one of the solo conditions was associated with negative parameter estimates, making the sum of the solo conditions inferior to their maximum.

In sum, all our analyses provide evidence that a network of brain regions including the left dorsal precentral gyrus shows evidence of integration during joint actions. However all these analyses also show that there is no overlap between regions showing evidence of integration and the putative mirror neuron system in the frontal lobe, and only restricted overlap in the parietal lobe and higher-level visual areas. Although one might argue that relaxing statistical thresholds or increasing the statistical power of the experiment might reveal overlaps between these networks in the frontal lobe, our results do suggest that the voxels most reliably associated with integration and the putative mirror neuron system differ.

Furthermore, as mentioned in the introduction, unlike imitation in the strict sense (Thorpe, 1956), in which the rule that links observed and executed actions is constant ('You do X so I do X'), joint actions often require changing this rule (Heyes, 2001; Iacoboni and Dapretto, 2006; Iacoboni et al., 1999; Newman-Norlund et al., 2007b). Relocating a dinner table for instance can involve changing from moving it sideways ('You move North so I move North') to turning it around ('You move North so I move South'). The integrative component of joint actions could therefore be split in two subprocesses: determining which rule is appropriate at a certain moment in time and then implementing this rule within the perception-action loop (Newman-Norlund et al., 2007a; Sebanz et al., 2006a). Given that our definition of joint actions is based on the *str* and *ang* blocks in which the rule stays constant across the 8 trials of a block, this definition will mainly capture voxels involved in *implementing* the rule, because processes involved in *determining* the rule would only occur once during a block and have a weak impact on the overall block activity. To capture brain areas involved in *determining* the rule, we additionally compared brain activity in the *mix* condition with the unmixed joint action blocks (contrast: *2mix>str+ang*). Figure S4 and Table S4 show that regions augmenting their blood flow when rules have to be changed more frequently (yellow) overlap with both putative mirror neuron system and sJA in the parietal (pink and brown, including part of the small overlap between putative mirror neuron system and sJA) but not the frontal lobe, pointing towards a functional dissociation between parietal and frontal nodes of both the putative mirror neuron system and sJA: while the frontal regions appear involved primarily in implementing the rule, the parietal regions seem also to participate in determining this rule.

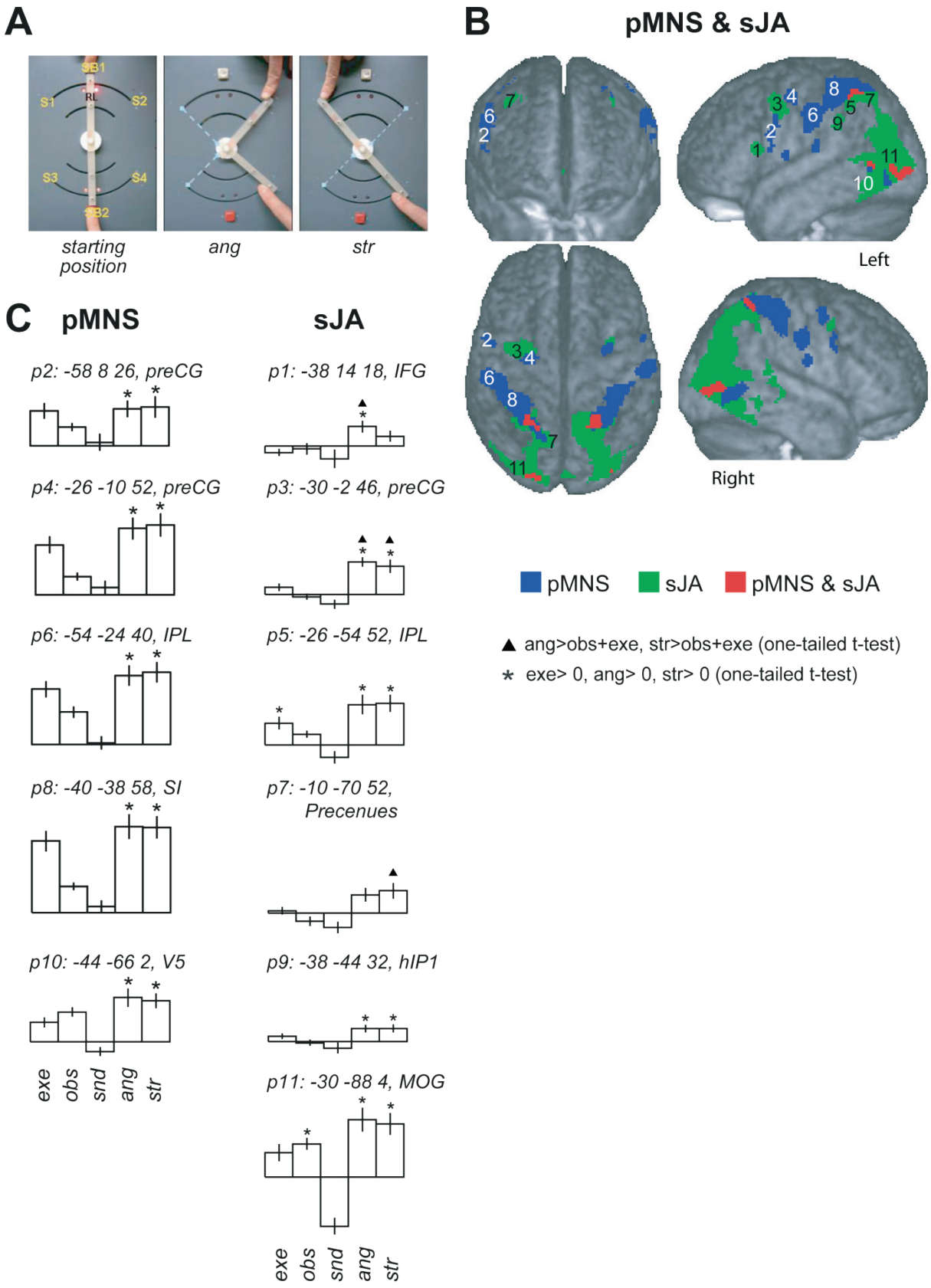


Figure 1: Experimental design and results. (**A**) left: photograph of the response box together with the fingers of the experimenter (top) and participant (bottom); middle: correct configuration for an angle trial, dotted lines showing alternative configuration; right: same for a straight trial. (**B**) Rendering of average brain of participants with pMNS (putative mirror

neuron system) (blue, *exe*>0 and *obs*>0, both p<0.001), sJA (Superadditive Voxels in Joint Actions) (green, a global null conjunction of *str>exe+obs+snd* and *ang>exe+obs+snd* inclusively masked with (*str>exe* and *str>obs* and *str>snd*) or (*ang>exe* and *ang>obs* and *ang>snd*) see Materials and Methods) and overlap between pMNS and sJA (red). Numbers refer to the location of peak parameter extraction in C. (**C**) parameter estimates of the peak locations in sJA and putative mirror neuron system in the left hemisphere, with 'p1' referring to peak location 1 in panel b and the triplet of numbers indicating the MNI coordinates of the peak. Parameter estimates were compared against zero (one tailed t-test) for *ang* and *str* condition in putative mirror neuron system regions (left column) and for *exe*, *obs*, *ang* and *str* for sJA regions (right column), and stars denote significant results. Finally, in all peak locations the comparison *ang-str* was not significant (two-tailed comparison). All comparisons thresholded at p<0.01 corrected for the number of peak locations in which the comparison was performed. All parameter estimates and the error bars (SEM) are shown on the same scale and can be directly compared (actual units irrelevant because arbitrary). Parameter estimates of right hemisphere are not shown because virtually identical.

2.3.2 Experiment II

While *Experiment I* determined a number of brain areas involved in *integrating* the observation of an external event with the execution of one's own actions, it cannot determine if this integration reflects joint actions in the strict sense, i.e. the mutual coordination of two agents. To examine this question, we scanned 8 participants again using a modified version of the game. Participants now used a joystick to manipulate a representation of the game box on the screen. This allowed us to contrast two conditions: (a) the participant played with a human agent that reacted to the participants own actions as in *Experiment I* and (b) the participant played with what he believed to be a computer, and which did not react to the participant's actions (see Materials and Methods and Figure S1E-H).

Debriefing of the participants after *Experiment II* confirmed that they felt they indeed played with the experimenter in condition (a) and with a computer in condition (b). They additionally commented that the experimenter was "friendlier" than the computer: only the human agent was perceived as cooperative whilst the computer, which they said "never waited for them", was not. All felt that using a joystick to control the game box made the task more difficult than using the 'real' game box of *Experiment I*. The average duration of the movement however was not different in the two conditions (2263ms in the human and 2115ms in the computer condition, t-test, p>0.42). The proportion correct trials (i.e. the experimenter and participant reaching the correct target location within 200ms of each other) was lower in the first session (human condition: 53% correct, computer condition: 56% correct), reflecting the initial difficulty in controlling the game box with the joystick, but improved in the remaining sessions, arriving at 69% correct overall for the human condition and 73.5% for the computer condition. Importantly, there was no significant difference between the performance in the two conditions (t-test, two-tailed, p>0.14).

We extracted in the peak voxel of the 12 ROIs identified in *Experiment I* (Figure 1), the activity during the straight and angle condition while participants played with the human agent and the computer, and analyzed the results using an ANOVA with 2 conditions (*str* vs *ang*), 12 ROIs and 2 agents (human vs. computer).

The main effect of Condition was not significant ($p>0.15$), nor did Condition interact with the other factors (all $p>0.09$). Reanalyzing the data using the sum of angle and straight in a 12 ROI x 2 Agents ANOVA revealed a main effect of Agent ($p<0.013$) with activity while participant played with the human agent being higher than when playing with a computer. In addition, there was a main effect or ROI ($p<10^{-7}$), and an interaction of ROI x Agent ($p<0.001$). Post-hoc comparison revealed that although activity was numerically larger for the human condition in all the ROIs of both the putative mirror neuron system and sJA, this difference was significant for dorsal frontal sJA (ROI3), ventral putative mirror neuron system (ROI2), the high level visual (ROI's 10 and 11) and many of the parietal regions (ROIs 6,7,8; see Figure 2, all $p<0.05$, one-tailed LSD-posthoc test).

In summary, both the putative mirror neuron system and sJA network were more responsive while playing with a human agent that responded to the actions of the participant, compared to playing with a computer that did not. This difference cannot be explained by the participants paying less attention to the actions of the computer, as the number of correct trials did not differ in the two conditions, nor can it be explained by differences in the time spent moving with the human agent or the computer, as the playing time did not differ significantly ($p>0.42$).

2.4 Discussion

Our aims were to identify the circuitry specifically involved during the task dependent *integration* of observed and executed actions that distinguishes joint actions from the action observation and execution done in isolation. In particular, we also aimed to examine the degree to which this process occurs within or beyond the putative mirror neuron system. In *Experiment I*, we found evidence for a distributed network of brain areas showing additional activity during joint actions compared to both the sum of solo observation and execution of similar actions (with or without taking the *snd* condition into account) and the maximum of solo *observation* and *execution*. As we predicted, this joint action network however overlaps remarkably little with the putative mirror neuron system, and not at all within the frontal lobe. In *Experiment II*, we found that in the joint actions and putative mirror neuron system networks, activity was stronger while participants played with a human agent that reacted to their own actions than while playing with a computer that did not.

In the following, we will first discuss the potential functional contribution of the main joint action clusters during *Experiment I*, and will assess critically how these findings constrain the role played by the putative mirror neuron system in our joint action task. Thereafter, we will discuss how *Experiment II* suggests that this activity is influenced by the presence of a social loop.

First, high level visual areas, including locations in the vicinity of the EBA (Downing et al., 2001) and STS (Puce and Perrett, 2003), are known to respond preferentially to the vision of biological agents and actions but also during blind action execution (Astafiev et al., 2004; Gazzola et al., 2006; Gazzola and Keysers, 2008; Gazzola et al., 2007a; Gazzola et al., 2007b; Iacoboni et al., 2001). The presence of these regions in our sJA and maxJA networks suggests that the process of integrating observed and executed actions may not only this integration may also

occur at a more sensory level. As suggested by the idea of forward models in motor control (Gazzola and Keysers, 2008; Wolpert et al., 2003; Wolpert and Ghahramani, 2000), the intended actions of the participant could be transformed into expected sensory consequences in high level visual cortex which can then be compared and integrated with the observed actions of the other. Alternatively, the need to act based on observing the other individual's actions may have heightened selective visual attention to both agents' actions during joint actions, causing part or all of the enhanced BOLD response in these regions. Such visual attention however would not be an epiphenomenon, but a functionally important mechanism to ensure optimal visual processing for action. Figure S3 shows that excluding the *snd* condition from the definition of sJA limits but does not abolish the involvement of these regions in joint actions, suggesting that the contribution of high level visual areas to joint actions, be it integrative and/or attentional in nature, is genuine.

Second, the putative mirror neuron system is known to transform the vision of actions into motor representations of similar actions (Etzel et al., 2008; Gallese et al., 2004; Gazzola and Keysers, 2008; Iacoboni and Dapretto, 2006; Keysers and Gazzola, 2006; Liepelt et al., 2008b; Rizzolatti and Craighero, 2004). Accordingly, it represents both partners' actions in a common code (Prinz, 1997) that is probably motor in the premotor regions but could be somatosensory or visual in other regions of the putative mirror neuron system (Gazzola and Keysers, 2008). In our task, during joint actions, the activity of the putative mirror neuron system was simply the sum of its activity during *obs+exe* or *obs+exe+snd*. This finding suggests that the activity observed in the putative mirror neuron system during joint actions appears to reflect two additive processes. During execution, activity in premotor and parietal regions probably reflects motor planning, while in high-level visual areas it may reflect the transformation of motor plans in the expected visual consequences of these actions using forward models. During observation, activity in high-level visual areas probably reflects processing of the visual stimulus itself while parietal and premotor activations would reflect activation of corresponding motor plans through inverse models (Gazzola and Keysers, 2008). *Experiment I* shows that in these regions, there is however no evidence for any additional, integrative processing between the streams of information corresponding to the two agents' actions. Neighboring areas of the sJA network may instead be responsible for these additional processes. This finding apparently contrasts with reports showing that the "mirror neuron system is activated to a greater extent during execution of actions carried out with a partner as compared to actions carried out alone" (Newman-Norlund et al., 2008). These authors however did not map the putative mirror neuron system in their participants, and their IFG cluster (47/16/25) fell outside of the putative mirror neuron system in our study.

A challenge for motor control during joint actions is the fact that our visual and motor systems have relatively long latencies (several hundreds of milliseconds). Our actions would thus lag behind those of our partner. An interesting property of the mirror neuron system however is that it is known to anticipate future actions that are not yet fully visible (Umilta et al., 2001). Motor control would then not react to an outdated representation of what the other person did several hundreds of milliseconds ago, but to an anticipation of his future actions, and the mirror neuron system would thereby contribute to solve this time lag issue (Kilner et al., 2004; Urgesi et al., 2006).

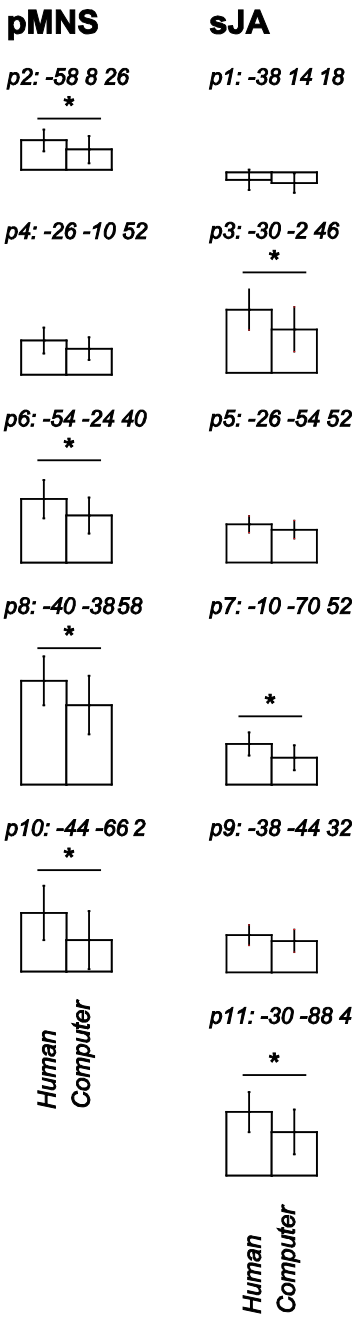
The lack of additional activity in the putative mirror neuron system during joint actions compared to solo actions suggests that this anticipation is triggered spontaneously both during solo observation and during joint actions.

Third, a large network including the posterior parietal lobe (inferior and superior parietal lobule; precuneus), the basal ganglia and cerebellum showed enhanced activity in joint actions. These areas are known to act in concert when monkeys and humans learn and use novel sensory-motor associations whether they involve other biological agents or not (Gold and Shadlen, 2007; Hikosaka et al., 2002). This network could therefore be crucial for transforming the novel and changing task requirements of our game into an appropriate way to map observed onto executed actions. The increase of activity in the mixed condition in the parietal location of this network would support the idea that this node is particularly involved in transforming the task requirement into an appropriate visuo-motor link.

Finally, the set of ventral and dorsal frontal clusters anterior to the putative mirror neuron system do not respond during execution or observation and therefore seem neither mirror nor premotor. The absence of responses during the vision of actions, and the absence of enhancement in the mixed compared to the unmixed conditions in these areas, make it unlikely that the preferential response during joint actions reflects the effect of visual attention or attentional memory load alone. Given that the rostral BA44 also contains regions responding during imitation but not observation or execution of finger movements (Molnar-Szakacs et al., 2005), this suggests that integrating two agents' actions recruits brain regions just anterior to the precentral and inferior frontal regions involved in motor control. This proximity would enable these regions to integrate very closely with the motor control and sensory functions ascribed to premotor areas in general and the putative mirror neuron system in particular. The detailed selectivity pattern of these regions and the nature of the computations they perform will however need to be addressed in future experiments.

By examining the results of *Experiment I* alone, we know that sJA areas are involved in the integration of a visual input and a motor output, but we cannot know if this integrational activity is specific for the *mutual* coordination that defines joint actions or would be just as strong during a task only requiring one-way coordination. In *Experiment II*, we therefore acquired brain activity in the ROIs of *Experiment I* in half of our participants while they played the same cooperation game with either a human agent that reacted to their own actions (mutual coordination) or (with what they thought to be) a computer, that did not (one-way coordination). Importantly, throughout the sJA and putative mirror neuron system ROIs, activity was higher while playing with the human agent, as demonstrated by the significant main effect of agent. This shows that despite the presence of biological movement in both conditions (given that a human experimenter blind to the participant's actions was actually playing the role of the computer), the presence of a human finger in the display, the belief to be playing with a human agent and/or the contingency that participants detected between the human agent and their own actions (mutual coordination) must have made these networks sensitive to the presence of the social loop that characterizes joint actions (Liepelt et al., 2008a).

Figure 2: Parameter estimates of the peak locations of *Experiment I* during joint action with a human (human) and with a computer (computer) in *Experiment II*. Peaks are numbered as in Fig. 1C (numbers indicating the MNI coordinates of the peak). All parameter estimates and the error bars (SEM) are shown on the same scale and can be directly compared (actual units irrelevant because arbitrary). *: Significant one-tailed human>computer differences according to LSD post-hoc comparison.



The task dependent *integration* of action observation and execution during joint actions however would occur *outside* of the putative mirror neuron system, in accord with our hypothesis and the previous theoretical proposals (Newman-Norlund et al., 2007a).

In summary, a number of studies have suggested that the IFG is not only involved when we respond to the actions of others by doing the same as they do (imitation) but also when responding with complementary actions (Newman-Norlund et al., 2007b) or engaging in joint actions (Newman-Norlund et al., 2007a). This has lead to the idea that the putative mirror neuron system would be responsible for integrating one's own actions to those of others in joint actions. In contrast, we hypothesized that the flexibility required during joint actions goes beyond the known properties of the mirror neuron system. Supporting our hypothesis, we find brain regions to be involved in *integrating* observed and executed actions during the social loop of joint actions, but these regions are distinct from the putative mirror neuron system that is engaged during solo observation and execution. In contrast to recent claims, our data therefore suggest that joint action may be a dual process:

One set of areas (including the putative mirror neuron system) seems to 'simply' transform observed actions into representations of similar actions in the observer through a combination of forward and inverse models (Gazzola and Keysers, 2008). This ensures that the two essential components that need integration during joint actions are in the same neural code: our own actions and those of others. This code can be relatively motor, sensory or hybrid in different regions of the brain (premotor, STS or parietal), and the translation between these codes could depend on the forward and inverse models we build up while observing the consequences of our own actions and preparing the participant to act. This is compatible with the existing the animal literature (Fogassi et al., 2005; Gallese et al., 1996; Keysers et al., 2003; Kohler et al., 2002). In the monkey, this transformation predicts the goal of observed actions (Umilta et al., 2001), providing the observer with the opportunity to tune his actions to the *expected* actions of others instead of 'lagging behind' due to the latencies of the visual and motor system. Premotor neurons similar to the minority of 'logically connected' neurons in the macaque could serve to ensure that the participant now has a number of actions primed in his brain: actions both similar and complementary to those of the other individual.

The second set of areas showing additional activity during *integration* in joint actions then utilizes these common codes and behavioral alternative to integrate flexibly our own actions with those of others and select the most adequate action, amongst the alternatives primed in the premotor cortex, to achieve our current joint goals.

Further research investigating the functional connections between the two networks will shed more light on the roles of these distinct, but probably communicating, networks in one of our most defining features: our capacity to cooperate constructively with other members of our species.

Supplementary Figures

Figure S1: Stimuli used in *Experiment I* (A-D), and II(E-H). (A) Photograph illustrating the experimental setup. (B) Photograph of the response box. S1-S4 indicate the positions of the target sensors, SB1 and SB2 the starting buttons of the experimenter and participant, respectively, and RL the red light that was on while the experimenter pressed the SB1. (C) Target configuration in an angle trial with the dotted line illustrating the second possible configuration. (D) Same for a straight trial. (E) Computer display of a target configuration in a human angle trial. (F) Same for a computer trial. (G,H) same for straight trials.

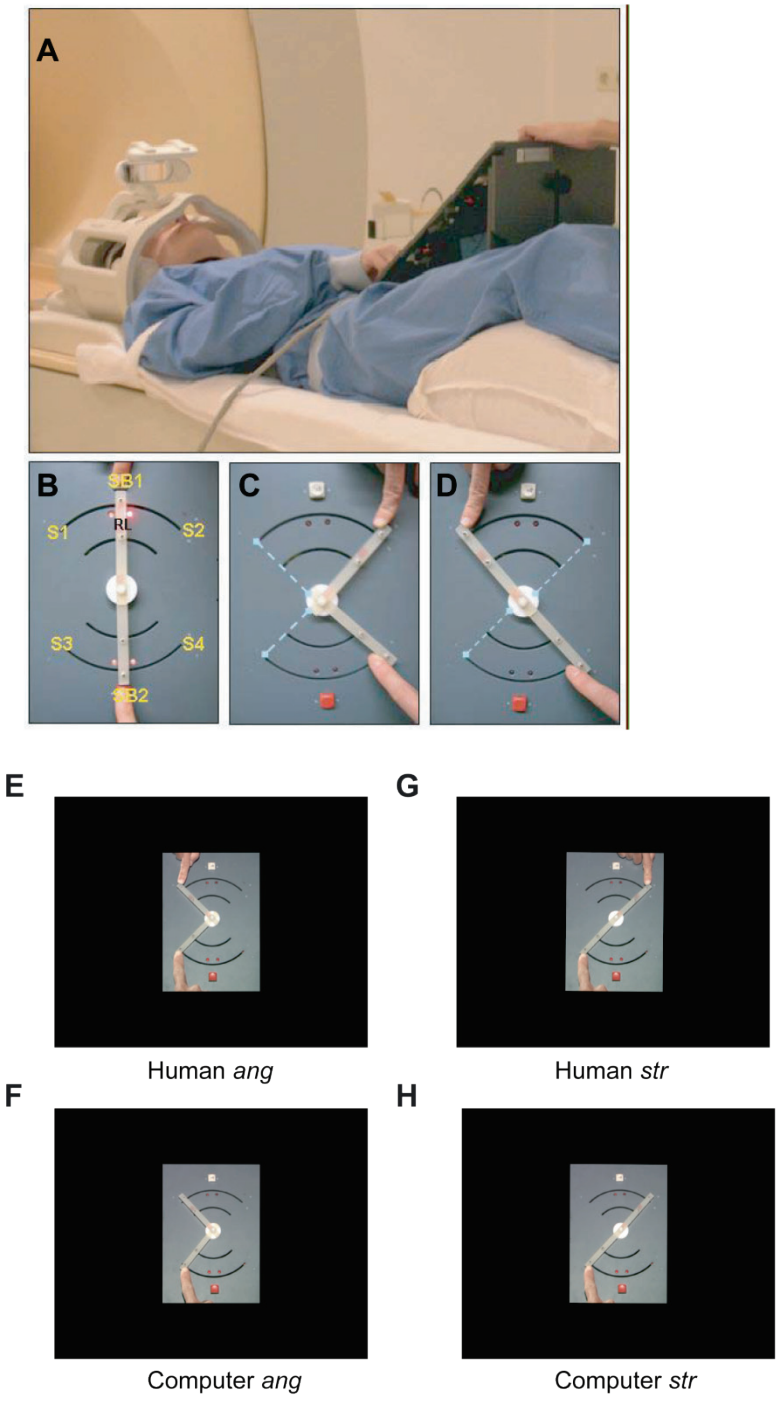


Figure S2: Timing of the conditions from the participant's perspective. For each of the six types of conditions (shown below each other, each as a patterned box), the time course of the auditory instructions (PAI) is given together with the appropriate timing of the participant's execution of the actions on the response box (PAct) and the observed actions of the experimenter (EAct). Light bulbs finally symbolize the on and off transitions of the red light of the experimenter. Note how the three time lines of the conditions involved joint actions (top three conditions) are the sum of the time lines of the three control conditions (bottom three conditions), except for the pre-trial instructions that do not flow into the analyses. This additivity is the basis for the definition of sJA voxels (e.g. *ang>exe+obs+snd*).

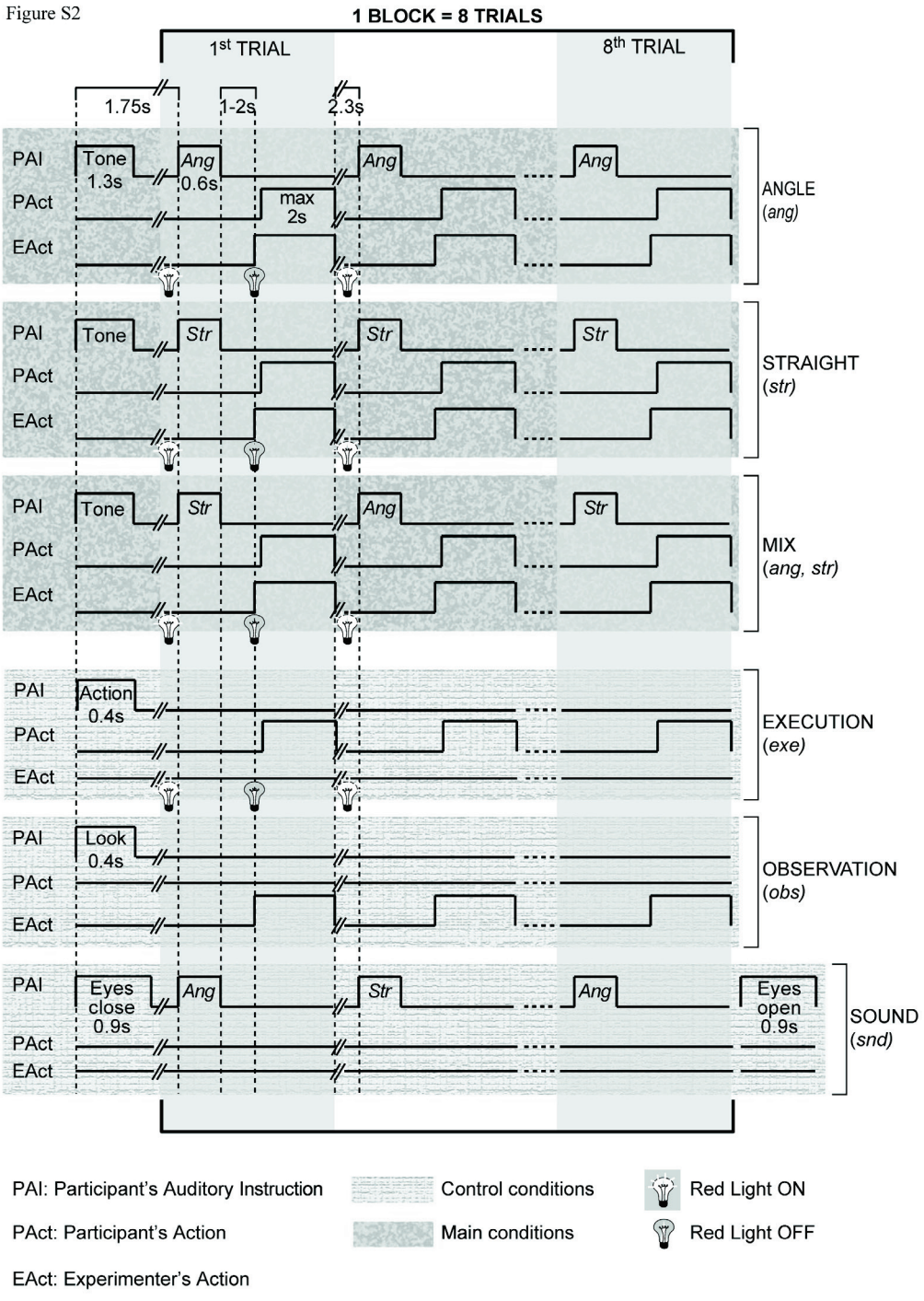


Figure S3: sJA analysis excluding the snd condition. (A) Rendering of average brain of participants with putative mirror neuron system (blue, exe>0 and obs>0, both p<0.001), sJA' (green, a global null conjunction of str>exe+obs and ang>exe+obs inclusively masked with (str>exe and str>obs) or (ang>exe and ang>obs) see Materials and Methods; the prime after sJA reflects the use of the alternative definition). The overlap between pMNS and sJA' did not reveal any results. The location of the peak is indicated with a red circle. (B) Parameter estimates of the representative peak location and the triplet of numbers indicating the MNI coordinates of the peak. Parameter estimates were compared against zero (one tailed t-test) for ang, str, exe and obs conditions, and stars denote significant results. The contrast 2mix-str+ang>0 (one-tailed t-test) and ang-str (two-tailed comparison) were not significant. All comparisons were thresholded at p<0.01. The parameter estimates and the error bars (SEM) are shown on the same scale and can be directly compared (actual units irrelevant because arbitrary).

Figure S3

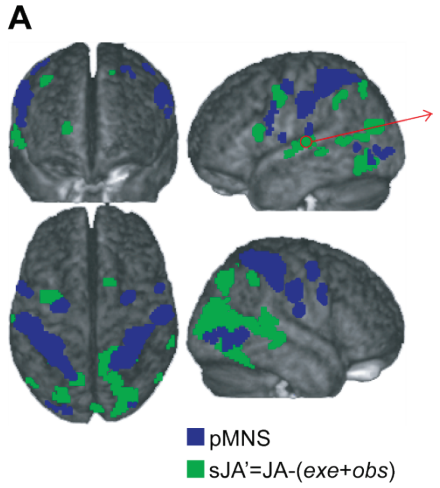


Figure S4

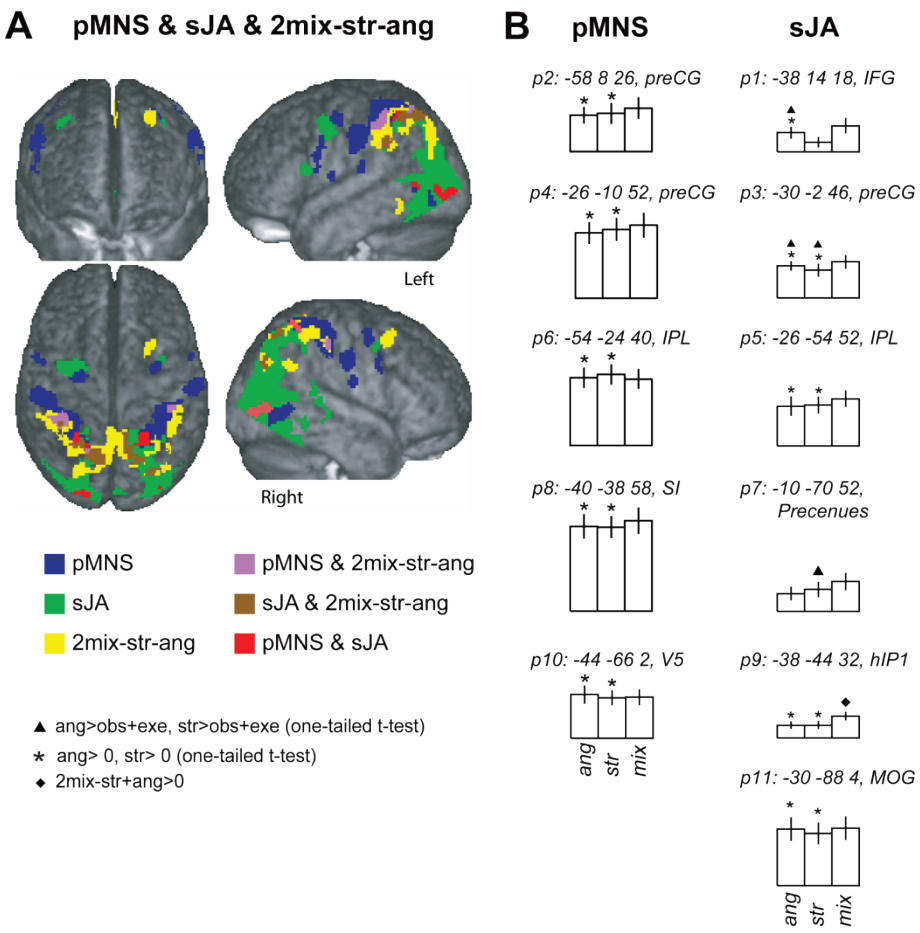
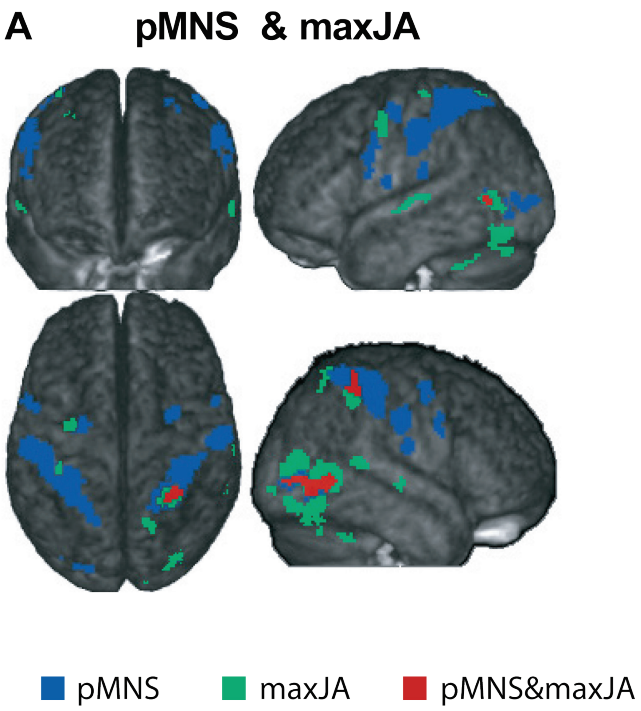


Figure S4: (A) Overlap of sJA and pMNS with *2mix-str-ang* as specified in the legend. (B) Parameter estimates of the peak locations in sJA, pMNS and *2mix-str-ang* contrast. Parameter estimates were compared against zero (one tailed t-test) for *ang* and *str* and stars denote significant results. The contrast *2mix-str+ang*>0 (one-tailed t-test) was tested in all locations an significant results marked with a diamond. All comparisons thresholded at p<0.01 corrected for the number of peak locations in which the comparison was performed. All parameter estimates and the error bars (SEM) are shown on the same scale and can be directly compared (actual units irrelevant because arbitrary). Parameter estimates of right hemisphere are not shown because virtually identical.

Figure S5: (A) Rendering of average brain of participants with putative mirror neuron system (blue, exe>0 and obs>0, both p<0.001), maxJA (green, a global null conjunction of str>max (exe,obs) and ang>max (exe+obs) see Materials and Methods) and the overlap between pMNS and maxJA (red).



Supplementary Tables

Table S1. Putative Mirror Neuron System

Results of inclusively masking the contrast *obs*-baseline with *exe*-baseline, both at p<0.001 uncorrected (all survive false discovery rate correction at p<0.05). Only clusters of 10 voxels or more are reported. For each cluster, its size in voxels and hemisphere are indicated first. For each of the subpeaks of the cluster, the cytoarchitectonic areas (based on the anatomy toolbox ((Eickhoff et al., 2005)) for SPM) followed by their MNI coordinates and t-value are reported. The t-value represents the t-value during *obs*. See Table S5 for abbreviations.

Size (vox)	Hem	Area	x	y	z	t
1066	L	SI	-40	-38	58	7
		PF	-46	-24	36	5.48
		Precuneus	-16	-66	60	4.95
		SPL				
739	R	SPL	30	-52	66	9.17
		SI	32	-50	64	8.68
305	R	MTG/V5	48	-62	4	9.71
		MOG	28	-88	2	9.44
		V3	32	-90	0	8.68
		ITG				
168	R	SI	56	-16	38	5.67
		PF				
127	L	MOG	-26	-90	-2	7.96
		V1				
87	L	BA6/preCG	-26	-10	52	5.56
		MFG				
66	R	MFG	30	-2	56	4.64
50	L	BA44	-58	8	26	5.6
		BA6	-56	4	34	4.38
48	R	PF	60	-12	22	4.3
		SI	56	-12	26	4.23
		SII(OP4)				
39	L	SII(OP1)	-48	-28	18	7.16
30	L	V5	-44	-66	2	6.2
28	R	BA6	56	6	40	4.42
		preCG	58	8	30	3.96
22	L	Insula/SII	-40	-6	12	4.76
16	L	MOG	-48	-76	-2	8.72

Table S2. Superadditive Voxels in Joint Actions

Results of global null conjunction ang>exe+obs+snd and str>exe+obs+snd at p<0.001 uncorrected (all survive false discovery rate correction at p<0.05) inclusively masked with ((ang>exe and ang>obs and ang>snd) or (str>exe and str>obs and str>snd)) at p<0.05 uncorrected as outlined in the Materials and Methods section 'sJA'. Only clusters of 10 voxels or more are reported. For each cluster, its size in voxels and hemisphere are indicated first. For each of the subpeaks of the cluster, the cytoarchitectonic areas followed by their MNI coordinates and t-value of the global null conjunction are reported. See Table S5 for abbreviations. Note: given that the t-value of a global null conjunction reflects the minimum t of the two contrasts that are examined, all peaks with a minimum t-value of 1.92 or higher also survive a conjunction requiring that both the ang and the str are above the sum of their controls (see (Gazzola et al., 2006)).

Size (vox)	Hem	Area	x	y	z	t
6199	L	FusiformG	-28	-66	-14	10.28
	L	BA 17	-12	-94	2	9.21
	R	SOG	32	-88	12	9.09
	L	BA 18	-14	-96	6	9.09
	L	IOG	-32	-86	-2	8.06
	R	V3	22	-84	-6	8.39
	L	V4	-20	-80	-12	8.19
	R	MOG	30	-80	18	8.06
	R	BA 18	10	-70	-10	7.45
	R	V4	32	-72	-12	7.4
	R	IOG	34	-78	-8	6.95
	L	Cerebellar Vermis	-2	-78	-12	6.54
	R	Cerebullum	10	-60	-12	6.46
	R	Precenues	8	-56	60	5.96
	R	FusiformG	24	-68	-14	5.59
	L	Precenues	-10	-70	52	5.1
	R	Cerebellar Vermis	6	-62	-20	4.89
	L	IPL	-26	-54	52	4.32
	R	MTG	46	-58	14	4.2
	L	Cerebellum	-18	-64	-20	3.25
	L	SPL	14	-70	54	3.17
	L	MTG	-52	-56	8	2.18
1847	L	Hippocampus	-22	-32	-2	6.95
	R	Thalamus	10	-22	10	5.84
	L	Thalamus	-8	-18	14	5.26
	R	STG	44	-32	2	3.08
288	L	preCG	-30	-2	46	3.95
74	L	Pallidum	-12	-2	-2	5.1
71	L	hIP1	-36	-44	34	3.08
48	L	IFG	-38	16	18	4.48
45	R	IPC	58	-42	16	3.5
35	R	ITG	50	-48	-6	3.08
28	R	preCG	36	4	48	2.84
13	L	Putamen	-20	12	-6	2.47

Table S3. The overlap between sJA and pMNS

Only clusters of 10 voxels or more are reported. For each cluster, its size in voxels and hemisphere is indicated first. For each of the subpeaks of the cluster, the cytoarchitectonic areas followed by their MNI coordinates and t-value in the global null conjunction of sJA are reported. See Table S5 for abbreviations.

Size (vox)	Hem	Area	x	y	z	t
127	L	IOG	-32	-86	-2	8.6
	L	MOG	-26	-92	2	8.1
110	R	MOG	36	-82	0	7.65
36	R	SPL	18	-54	62	2.59
25	L	SPL	-26	-54	56	3.17
14	L	MTG	-42	-66	6	2.51

Table S4. Comparison of mixed and unmixed joint action conditions

The contrast (*2mix>str+ang*) at p<0.001 uncorrected (all survive false discovery rate correction at p<0.05).Only clusters of 10 voxels or more are reported. For each cluster, its size in voxels and hemisphere is indicated first. For each of the subpeaks of the cluster, the cytoarchitectonic areas followed by their MNI coordinates and t-value are reported. See Table S5 for abbreviations.

Size (vox)	Hem	Area	x	y	z	t
1410	L	IPL	-36	-42	44	9.28
	L	hIP2	-42	-40	36	6.25
	L	Precuneus	-14	-64	58	6.17
	L	MOG	-28	-78	38	5.61
	R	Precuneus	8	-60	60	5.53
	L	SPL	-24	-58	54	5.47
	L	IPC/PF	-56	-38	42	4.61
	R	SPL	14	-74	54	3.98
120	R	SI	44	-42	60	5.23
	R	IPL	42	-48	52	4.33
	R	SPL	42	-50	58	4.23
82	R	MFG	26	14	56	5.14
	R	SFG	28	16	58	4.83
70	R	SOG	26	-80	38	4.77
	R	IPC	38	-74	34	3.98
43	R	AngularG	42	-56	34	4.89
24	L	ITG	-52	-54	-14	4.73
16	R	Thalamus	16	-26	10	4.46

Table S5. Abbreviations used in the paper together with their meaning

All brain areas were labeled using the Anatomy Toolbox for SPM (Eickhoff et al., 2005), with areas preceded by a '*' based on probabilistic cytoarchitectonic maps

	ang	angle joint action condition
	AngularG	angular gyrus
*	BA 17	Brodmann area 17
*	BA 18	Brodmann area 18
*	BA44	Brodmann area 44
*	BA6	Brodmann area 6
	BOLD	blood-oxygen-level dependent
	EBA	extrastriate body area
	EPI	echo-planer imaging
	exe	execution condition
	fMRI	functional magnetic resonance imaging
	FusiformG	fusiform gyrus
	GLM	general linear model
	Hem	hemisphere
*	hIP1	human intraparietal area 1
*	hIP2	human intraparietal area 2
	IFG	inferiror frontal gyrus
	IOG	inferior occipital gyrus
	IPC	inferior parietal cortex
	IPL	inferior parietal lobule
	ITG	inferior temporal gyrus
	jaHA	joint action human agent
	jaNHA	joint action non-human agent
	maxJA	joint action voxels calculated using a maximum requirement, i.e. ang> max (exe,obs) OR str> max (exe,obs).
	MFG	middle frontal gyrus
	mix	mixed joint action condition
	MOG	middle occipital gyrus
	MTG	middle temporal gyrus
	obs	observation condition
*	PF	Parietal area F
	pMNS	putative mirror neuron system, i.e. obs>0 AND exe>0
	preCG	precentral gyrus
	RL	red light
	ROI	region of interest
	SB	start button
	SFG	superior frontal gyrus
	SI	primary somatosensory area
	SII	secondary somatosensory area
*	OP1	operculum parietale 1
*	OP4	operculum parietale 4
	sJA	superadditive voxels in joint actions, i.e. ang>exe+obs+snd OR str>exe+obs+snd
	snd	sound condition
	SOG	superior occipital gyrus
	SPL	superior parietal lobule
	STG	superior temporal gyrus
	str	straight joint action condition
	STS	superior temporal sulcus
	V1	primary visual area
	V3	extrastriate visual area 3
	V4	extrastriate visual area 4
	V5	extrastriate visual area 5
	Vox	voxel

Table S6. Alternative definition of sJA excluding the *snd* condition (sJA')

Results of global null conjunction *ang>exe+obs* and *str>exe+obs* at p<0.001 uncorrected (all survive false discovery rate correction at p<0.05) inclusively masked with ((*ang>exe* and *ang>obs*) or (*str>exe* and *str>obs*)) at p<0.05 uncorrected as outlined in the Materials and Methods as the alternative definition of sJA. Only clusters of 10 voxels or more are reported. For each cluster, its size in voxels and hemisphere are indicated first. For each of the subpeaks of the cluster. The cytoarchitectonic areas followed by their MNI coordinates and t-value of the global null conjunction are reported. See Table S5 for abbreviations. Note: given that the t-value of a global null conjunction reflects the minimum t of the two contrasts that are examined. all peaks with a minimum t-value of 1.92 or higher also survive a conjunction requiring that *both* the *ang* and the *str* are above the sum of their controls (see (Gazzola et al., 2006)).

Size (vox)	Hem	Area	x	y	z	t
1124	R	IPC	62	-40	12	4.64
		V1	24	-92	16	3.99
		PF	58	-38	10	3.90
		V5	48	-58	14	3.39
		V3	20	-94	2	3.23
		Thalamus	6	-20	10	2.94
		Hippocampus	10	-26	12	2.77
		STG	46	-38	12	2.77
573	R	Cerebeller Vermis	6	-50	-6	5.57
	R	Cerebellum	14	-48	-20	4.50
	L	Cerebellum	-6	-56	-8	3.28
	L	V1	-6	-52	-8	3.28
567	R	V3	6	-74	-10	7.21
		V1	10	-70	-10	7.13
		V2	2	-76	-10	6.69
		V4	22	-70	-14	5.23
149	L	preCG	-30	-2	46	3.99
147	L	OP4	-60	-18	2	7.16
		TE1	-56	-10	-2	6.73
		OP1	-56	-30	6	4.87
		IPC	-38	-30	10	3.17
136	R	Precenues	8	-54	58	4.50
		SII	8	-54	58	2.77
117	L	V4	-22	-76	-12	4.55
		V3	-20	-80	-12	4.36
		V5	-30	-76	-4	2.55
108	R	Precenues	16	-68	44	4.87
75	L	V2	-2	-84	-6	5.23
	R	V1	6	-88	-6	5.04
54	L	Putamen	-22	16	4	3.28
45	L	Precenues	-12	-70	48	4.44
43	L	hIP1	-30	-50	40	3.62
36	L	Thalamus	-6	-16	16	3
35	L	Hippocampus	-22	-30	-2	3
27	L	BA44	-40	16	18	3.25
23	R	hIP1	34	-50	46	2.43
11	R	preCG	16	10	56	2.52

3. Granger Causality Mapping During Joint Actions Reveals Evidence for Forward Models That Could Overcome Sensory-Motor Delays

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ABSTRACT

Studies investigating joint actions have suggested a central role for the putative Mirror Neuron System (pMNS) because of the close link between perception and action provided by these brain regions (Knoblich and Jordan, 2002; Newman-Norlund et al., 2007a; Newman-Norlund et al., 2007b). In contrast, our previous functional magnetic resonance imaging (fMRI) experiment demonstrated that the BOLD response of the pMNS does not suggest that it directly integrates observed and executed actions during joint actions (Kokal et al., 2009). To test whether the pMNS might contribute indirectly to the integration process by sending information to brain areas responsible for this integration (integration network), here we used Granger causality mapping (GCM) (Roebroeck et al., 2005). We explored the directional information flow between the anterior sites of the pMNS and previously identified integrative brain regions. We found that the left BA 44 sent more information than it received to both the integration network (left thalamus, right middle occipital gyrus and cerebellum) and more posterior nodes of the pMNS (BA2). Thus, during joint actions, two anatomically separate networks therefore seem effectively connected and the information flow is predominantly from anterior to posterior areas of the brain. These findings suggest that the pMNS is involved indirectly in joint actions by transforming observed and executed actions into a common code and is part of a generative model that could predict the future somatosensory and visual consequences of observed and executed actions in order to overcome otherwise inevitable neural delays.

3.1. Introduction

Joint action is defined as the coordination of the actions of two or more individuals in time and space in order to bring about a change in the environment (Sebanz et al., 2006a). The neural circuitry behind joint actions has recently been investigated in a number of fMRI studies (Kokal et al., 2009; Newman-Norlund et al., 2008; Newman-Norlund et al., 2007b; Sebanz et al., 2006b). Most of these studies (Newman-Norlund et al., 2008; Newman-Norlund et al., 2007b; Sebanz et al., 2006b) found that the inferior frontal gyrus (IFG) and inferior parietal lobule (IPL), forming the best studied nodes of the putative mirror neuron system (pMNS), were active when participants engage in different sorts of joint action tasks compared to solo conditions, and have therefore argued that the pMNS could underlie our ability to

engage in joint actions (Newman-Norlund et al., 2008; Newman-Norlund et al., 2007b; Sebanz et al., 2006b) .

Strictly speaking however, we still know little about the contribution of the pMNS in joint actions as the aforementioned experiments (Newman-Norlund et al., 2008; Newman-Norlund et al., 2007b; Sebanz et al., 2006b) have merely deduced that their activations belong to the pMNS based on the macro-anatomical location of activation. Whether these regions are indeed also active while simply viewing and simply performing motor actions (the definition of the MNS) was not tested in these studies. Given that much of the IFG and IPL does not contain mirror neurons, it is difficult to interpret whether the brain regions in the IFG and IPL identified in these studies are really part of the pMNS, and hence whether the pMNS contributes to joint actions (Kokal et al., 2009; Thioux et al., 2008).

In order to test the contribution of the pMNS in joint actions more directly, we performed an fMRI experiment in which the pMNS was mapped in addition to mapping regions selectively involved in the integration of the participants' actions with those of the experimenter during joint actions (Kokal et al., 2009). Participants engaged in joint actions with an experimenter who was standing next to them by creating geometrical shapes in real-time. Participants additionally performed the same actions singly (execution) and observed the experimenter's actions (observation). Consequently, we could identify the common voxels for both execution and observation in order to map the pMNS of our participants. The pMNS was identified in the IFG, precentral gyrus, parietal regions (SI, SII, SPL, see Table S1 for abbreviations) and middle temporal gyrus (MTG) bilaterally (Fig. 1A, blue). We then identified areas where the activity in joint actions exceeded that during the sum of solo execution and observation given that engaging in joint action additionally requires partners to *integrate* solo execution and observation (if integration >0 then joint action = observation + execution + integration)> observation + execution). The areas responsible for this *integration* process were located bilaterally in the IFG, precentral gyrus, SPL, IPL, middle and temporal occipital gyri and cerebellum (Fig. 1A, green). Lastly, we checked whether this integration network overlapped with the pMNS to test whether the pMNS directly contributes to joint actions by integrating observed and executed actions. This analysis, however, revealed only very restricted overlap in the SPL and the high-level visual areas (Fig. 1A, red). Indeed, the frontal areas of the integration network in the IFG did not fall in the pMNS. Neither were the anterior sites of the pMNS showing evidence of integrative processes during joint actions. Therefore, this suggested that the anterior sites of the pMNS do not play a *direct* role in the integration of observed and executed actions in joint actions (Kokal et al., 2009). Instead, we hypothesized that the anterior pMNS sites still contribute to joint actions by transforming observed and executed actions into a single code (Etzel et al., 2008), and then sending this information to regions performing the integration, but not by directly performing the additional integration needed in order to respond with appropriate actions to those of the observed partner (Kokal et al., 2009).

In order to test this hypothesis, here we explore the directional influences between brain areas of the pMNS and the integration network using Granger causality mapping (GCM), which has recently been used to map effective connectivity in the human brain (Goebel et al., 2003; Jabbi and Keysers, 2008; Roebroeck et al., 2005;

Schippers et al., 2010). To maximize the statistical power of this analysis, we did not calculate GCM for the entire brain, but only in the regions that can inform our question: between the anterior sites of the pMNS and the integration network (to examine information flow between the pMNS and integration network) and the posterior sites of the pMNS (to examine information flow within the pMNS) on our fMRI data. All regions were identified in our previous experiment (Kokal et al., 2009).

Firstly, in accord with our hypothesis, our results suggest that these two functionally separate networks were effectively connected. Secondly, this information flow was predominantly backwards (from anterior to posterior regions of the brain) which is compatible with generative models emphasizing that the premotor areas may actually send more predictions to the sensory areas than the other way around. We propose that overcoming the sensory delays by relying on the predicted actions of others could be beneficial when engaging in joint actions which entail the tight temporal coordination of two actors.

3.2. Materials and Methods

We employed Granger causality mapping on fMRI data collected for a previous experiment (Kokal et al., 2009). Temporal information in the data was used to measure the influences between brain regions without an apriority model of regional connections. The procedure of the fMRI experiment was published previously (Kokal et al., 2009). Here we report the relevant details for this study only:

Participants: 18 healthy volunteers; all right-handed; 10 female and 8 male; mean age 23.7 years ranging 20-45 years with normal or corrected to normal vision and without a history of neurological, major medical, or psychiatric disorders. The experiment was approved by the Medical Ethical Commission of the University Medical Center Groningen, the Netherlands. Participants gave informed consent and were paid for their participation.

Procedure: In the fMRI session, the participant played a cooperation game with the experimenter who was standing next to the participant (joint actions) or performed one of two non-cooperative control conditions (solo execution and solo observation)

1) *Joint Action*: The experimenter and the participant together shaped the two sticks of a game box in either an ‘angle’ or a ‘straight’ line (see Fig. 1B and Video S1). Each stick was controlled by a different player: the lower stick was controlled by the participant and the upper one by the experimenter. In the beginning of each trial, players had to press their respective start buttons and hold their right index fingers there (SB1 and SB2 in Fig. 1B) until the experimenter started to move her stick. In the meantime, each of them received different auditory instructions: the experimenter received auditory instructions indicating where (left or right) she should move her stick; the participant received auditory instructions indicating the geometrical shape (an angle or a straight line) that they would need to create together. Between 1 and 2s (random interval) after the participant had received the angle or straight instruction the experimenter was instructed with a ‘go’ signal. Immediately after this signal, she initiated the joint action by moving the upper stick to the left or right while the

participant had to react by starting to slowly move the lower stick in the direction suitable to achieve the target shape (Video S1). Likewise, the participant had to synchronize his actions closely with those of the experimenter to reach the target location virtually simultaneously (within 200 ms of each other) to jointly win the trial. This tight time constraint ensured that both players monitored and coordinated the velocity of their movements carefully and continuously throughout the trial, requiring both the spatial and temporal coordination that defines joint actions. Consequently, participants had to carefully watch the experimenter's actions to determine (a) *which side* to move and (b) *when* and how quickly to move.

2) *Execution (exe)*: In the joint action condition, a red light (RL in Fig. 1B) was turned on whenever the experimenter placed her finger on the start button (SB in Fig. 1B) and turned off whenever she left the SB to start her action. Likewise, in the execution condition, the experimenter's RL was turned on and off with the same timing as in the joint action conditions without the experimenter being visible. The participants were instructed to move their stick to the right or left whenever they saw the red light turn off on the box, ensuring that the timing of the participant's actions was the same as in the joint action blocks but not triggered by a biological action. The participants could choose what side to go to, but were instructed by the experimenter to avoid going to the same side constantly. At the end of both joint action and execution trials, they released their sticks and had to place their index finger back onto the starting buttons and wait for the auditory instructions of the next trial.

3) *Observation (obs)*: Participants were instructed to carefully watch the experimenter move her stick randomly to the right or left using the same timing as in a joint action block.

Different conditions were arranged in blocks of 8 trials separated by 2.3 s. Each trial lasted between 3.6 and 4.6s depending on the random interval between the auditory trial instruction and the initiation of the movement. Accordingly, each block lasted between 45 and 54s depending on these random intervals. Blocks were separated by 14 ± 2 s random pauses (including the verbal instruction or the sound indicating the type of block to follow). Each block started with a different auditory instruction presented 1.75 s before the block indicated the nature of the block: for the execution block 'action' (400 ms), for the observation block 'look' (400 ms) words were presented; for the joint action blocks a sine wave (440 Hz) tone was presented. The experiment also contained a sound only condition which was however not used in this GCM analysis.

Each run contained two blocks of each of the conditions and five runs (a total of 10 blocks of each condition) were acquired. The order of the conditions was counterbalanced between runs and participants. Stimuli were programmed and presented using the Presentation software (Neurobehavioral systems, Davis, CA). At the end of the each run, participants were informed about how successful they were in creating shapes in the joint action trials to convey a mutual feeling of cooperation.

Data acquisition: Imaging was performed with a Philips Intera 3T Quaser with a synergy SENSE head coil and maximum gradient strength of 30 mT/m. Head movements were minimized by using foam padding and never exceeded 3mm in a run. We used a standard single shot EPI with TE = 28 ms, TA= 1.25 s, TR= 1.3 s, 28 axial slices of 4 mm thickness, without slice gap and a 3.5x 3.5 mm in plane

resolution acquired to cover the cortex and most of the cerebellum. A T1 weighted structural scan was acquired with TR=15.31 ms, TE=3.6 ms, flip angle=8 deg.

Data preprocessing: Using SPM5 (www.fil.ion.ucl.ac.uk/spm) implemented in MATLAB 6.5 (Mathworks Inc., Sherborn, MA, USA). All EPI volumes were aligned to the first volume acquired for each participant and a mean EPI image generated after realignment. Spatial normalization was performed by co-registering the structural volume to the mean EPI, segmenting the coregistered structural image, determining the normalization parameters required to warp the gray matter segment onto the gray matter MNI template, and applying these parameters to all EPI and structural volumes. No spatial smoothing was applied on the functional data for the granger data, but smoothing had been used to calculate the traditional GLM published previously (Kokal et al., 2009) which served to delineate our regions of interest for the Granger analysis.

Traditional GLM analysis at the Single participant level: GLM was performed using separate auditory predictors for the conditions joint action condition to capture brain activity caused by hearing the words "angle" or "straight" and separate action predictor for the joint action, observation and execution conditions to capture brain activity triggered by executing and/or observing the finger movements. Each predictor was a boxcar function that reflected the trial-by-trial timing of the auditory and movement epoch of the condition. The boxcar functions were convolved with the haemodynamic response function, and fitted separately for each run to the data. In addition, the head motion and rotation along the three axes were entered as six covariates of no interest in the design matrix to single out motion artifacts although motion never exceeded 3mm within a run. Given that little time separated the auditory instructions from the actions within a block (average=1500 ms), the auditory and action predictors overlap in time (after convolution with the haemodynamic response function), and the attribution of a brain activity to one rather than the other was uncertain. Instead of analyzing the parameter estimates separately for the auditory and action predictor, we combined them by summing the surface under the fitted auditory and action predictors. This was done simply by multiplying the parameter estimates (Beta) obtained from the GLM with the surface (S) under their respective predictor ($S=Beta_{auditory}xS_{auditory} + Beta_{action}xS_{action}$). Brain activity across conditions were compared using this surface (for details please see (Kokal et al., 2009)).

Population analyses: To implement a random effect analysis, contrast estimates obtained separately for each participant were tested at the population level, using one-sample t-tests and ANOVA analyses testing whether the average contrast differs from zero. Only results that are significant both at $p < 0.001$ uncorrected and $p < 0.05$ corrected using false discovery rate are reported as significant. Only clusters of at least 10 voxels are shown.

pMNS (Putative Mirror Neuron System) definition: First, we compared the surface under the curve in *obs* against zero (t-test) and we did the same for *exe*, too. Later, only those voxels with significant results ($p<0.001$, uncorrected) in both analyses at the second level were identified and constituted the pMNS (i.e. $(Beta_{action}xS_{action})_{obs}>0$ & $(Beta_{action}xS_{action})_{exe}>0$, where & is a logical, both at $p_{unc}<0.001$ and $p_{fdr}<0.05$).

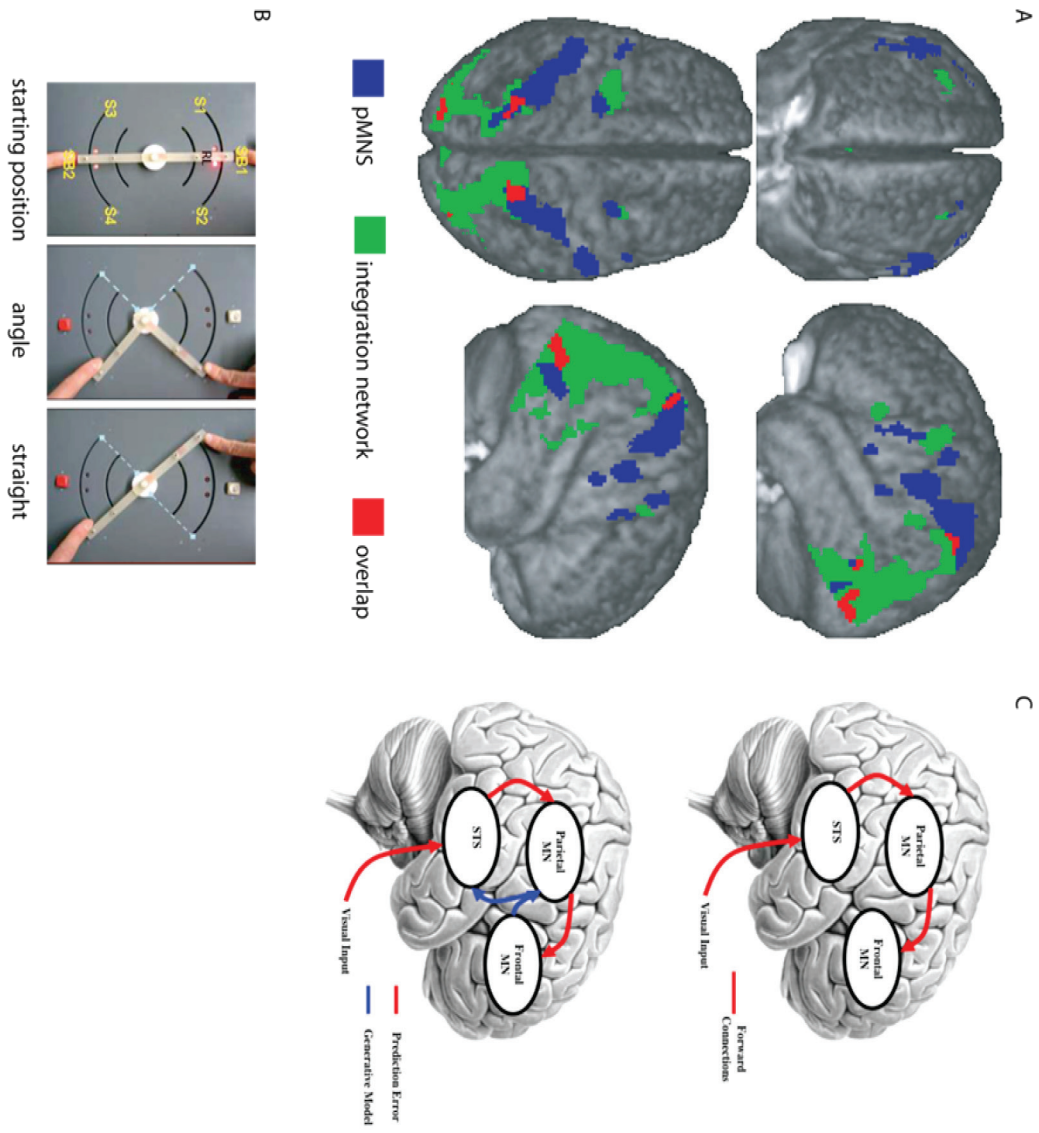


Figure 1: (A) The main results of the fMRI experiment: rendering of average brain of participants with pMNS (putative mirror neuron system) (blue, *exe*>0 and *obs*>0, both p<0.001), integration network (green) and overlap between two networks (red). For the color figure please see page 29. (B) The schemas of the mirror neuron system, showing the frontal and parietal sites of the mirror neuron system and STS as well as the inverse (recognition) model (red lines) and forward (predictive) model (blue lines) (C) The experimental set-up: (left) the photograph of the response box together with the fingers of the experimenter at the top and participant at the bottom; (middle) the correct configuration for an angle trial, dotted lines showing alternative configuration; (right) same for a straight trial.

Integration Network definition: To map the regions showing activity that indicates their contribution in integrating observed and executed actions, two contrasts were calculated for angle and straight joint actions by subtracting both *obs* and *exe* from joint actions with the surface analysis at the first level. Later 18 contrasts (one per participant) per joint action (*ang* & *str*) were entered in a one way ANOVA without constant, and the global null conjunction calculated to estimate the likelihood of the null hypothesis (m(C_{ang})<=0 & m(C_{str})<=0) that the voxel was not involved in either joint action (Friston et al., 2005). To prevent to accept the voxels in which the activity in angle (*ang*) or straight (*str*) was above the sum of execution and observation (*exe+obs)* without being above the activity in *exe* and *obs* individually, we required that these voxels fall within an inclusive mask where ((*ang>exe* and *ang>obs*) or (*str>exe* and *str>obs*)).

Single Subject Granger Causality Mapping (GCM): GCM is an effective connectivity method, which is based on the Granger causality concept to measure the existence and predominant direction of influence from information in time series (Roebroeck et al., 2005). The concept of Granger causality states that if a time series I_t has a causal influence on J_t, then fluctuations in I_t should consistently precede those in J_t. More specifically, I_t is thought to Granger cause J_t if taking I_{t-1} into account improves the capacity to predict J_t compared to only taking J_{t-1} into account. Here, differential Granger causality maps (dGCM) were computed for each source voxel with an order of 1 TR (1.3s) by computing the linear direct influence of source to target (I→J) and of target to source (J→I), and subtracting the latter from the former. This was done separately for the three block/conditions (joint action, execution and observation) using unsmoothed normalized data. All calculations were performed using an in-house program coded in MATLAB (The Mathworks, Natick, MA) which uses SPM5. The input to the program consisted of the time course of each source voxel (I) which was extracted using MarsBar (http://marsbar.sourceforge.net) and a binary temporal mask (M(t)) which had a value of 1 if this volume fell within an epoch to be included in that particular calculation and a 0 otherwise. Our in-house software then only used those volumes of the data for M(t) and M(t-1) has a value of 1 to calculate directed influences with an order of 1. The influence of region X on region Y was quantified by calculating two regressive models taking all t into account for which M(t)=M(t-1)=1. One predicting the present of variable Y only based on the past of Y itself: Y(t)=a*Y(t-1)+e(t); and one additionally taking the past of X into account Y(t)=a'*Y(t-1)+b*X(t-1)+e'(t). The influence of X→Y is then calculated as $F_{X\rightarrow Y}$=sd(e(t))/sd(e'(t)). This means that we essentially concatenated all repetitions of each type of block (total of 10 repetitions per condition in the experiment) and we used these concatenated time series to calculate the single autoregressive model but avoiding the borders between repetitions of the blocks where the Y(t) would be explained by values taken from a previous block acquired more than 1.3s ago. As recommended (Roebroeck et al., 2005), both the temporal mask was restricted to the steady state phase of each block (i.e. the volumes corresponding to 10 s after the block onset), and were calculated separately for the joint action condition, the solo execution and the solo observation condition.

Source Regions of Interests for the GCM Analysis: Based on our hypothesis, the anterior sites of the pMNS (in BA 44 and in BA 6) in the left hemisphere were

selected as source region of interests (ROIs) based on their task-dependent BOLD characteristics as identified as significant clusters in the random effects group analysis in our previously published analysis (Kokal et al., 2009). The labels for the clusters are based on the cytoarchitectonic areas (based on the anatomy toolbox (Eickhoff et al., 2005) for SPM). The details of the ROIs can be found in Table 6.

Second level differential GCM analysis: To directly test whether any voxels in the anterior left regions of the pMNS exchange information with other regions of the pMNS or integration network, we then performed the following second level analysis. We applied smoothing with a Gaussian kernel of 8 mm full-width at half maximum (FWHM) to all dGCM maps of all participants (which have been calculated using unsmoothed data) to account for differences in localization across participants. These were 26 dGCM for the BA 44 ROI and 22 dGCM for the BA 6 ROI for each participant, corresponding to each of the voxels in the two ROIs. The smoothed 26 dGCMs for all the voxels of the BA 44 ROI were then included in a one-way ANOVA with dependent variance in order to account for spatial autocorrelation between neighboring voxels. We then defined a separate t-contrast for each of the dGCM (corresponding to each of the n voxels within BA 44), and performed a global null conjunction including all these t-tests using SPM and the minimum t-statistics (Friston et al., 2005). This tests the null hypothesis that none of the voxels in BA 44 has a dGCM larger than zero. We used this procedure instead of simply using the average time course of the entire ROI to detect cases in which only some voxels within our ROI have significant non-zero dGC while controlling for the multiple comparison problem arising from testing n contrasts (for further details see (Friston et al., 2005)). Additionally, by explicitly masking this conjunction with a mask including all other regions of the pMNS and integration network, we directly tested whether BA 44 sends more information to than it receives from all other voxels in the pMNS or integration network. The same was performed using t-test examining if each dGCM was significantly smaller than zero to test if any voxel received more information from than it sends to any of the other regions of the pMNS and integration network. The same procedure was then performed for the BA 6 ROI, too. In addition, we calculated a direct comparison between differential Granger causality maps between the various conditions (i.e. joint action versus execution blocks and joint action versus observation blocks). All the procedure which was used for within condition calculation was same (as described above for an example ROI, BA 44,) except the following: by using ImCalc function of SPM we applied a subtraction between GCMs of different conditions (i.e. $GCMs_{\text{joint action}} - GCMs_{\text{execution}}$) for each voxel for all ROIs. The resulting difference GCMs then entered in one-way ANOVA. We threshold our results at $p < 0.001$ at the voxel level and corrected for multiple comparisons at $p < 0.05$ with false discovery rate (FDR) and used a minimum cluster size of 10 voxels. We then overlaid our results onto an average brain of our participants for displays. All results were threshold using FDR correction at $p<0.05$.

3.3. Results

The differential Granger Causality (dGC) was significantly above zero from at least some left BA 44 voxels (part of the pMNS) to bilateral BA2 voxels in the

somatosensory cortex (also within the pMNS) and to voxels of the right MOG, left thalamus, left cerebellar vermis and right cerebellum (within the integration network) when analyses were confined to the joint action blocks (Fig. 2A & Table 1). This suggests that some voxels in the left BA 44 sent significantly more information to some voxels of both the pMNS and the integration network than it received from voxels in these regions during joint actions. In addition, the dGC was significantly above zero from at least some voxels in left BA 6 (part of the pMNS) to voxels of the left cerebellar vermis (part of the integration network) when analyses were confined to the joint action blocks (Fig. 2B & Table 2). This suggests that some voxels in the left BA 6 influenced the left cerebellar vermis part of the integration network more than the other way around during joint actions.

On the other hand, when analyses were confined to the solo execution blocks, we found that the dGC was significantly above zero only from some left BA 44 to some right MOG voxels (Fig. 3A & Table 3). This suggests that during solo execution in which the participants moved their stick to left or right, parts of the left BA 44 sent significantly more information to parts of the right MOG, a high level visual area within the integration network, than it received. When analyses were confined to the observation blocks, we found that the dGC was significantly above zero only from some voxels of the left BA 44 to some voxels in the bilateral cerebellar vermi and left MOG (Fig. 3B & Table 4). Thus, during solo observation in which the participants observed the experimenter moving her stick to left and right, the left BA 44 sent significantly more information to two regions of the integration network in bilateral cerebellar vermi and left MOG than it received from them. We did not find any significant dGC above zero between the anterior and posterior sites of the pMNS when analyses were confined to the observation and execution blocks.

In addition, a direct comparison between differential Granger Causality maps (dGCMs) calculated for the various conditions (i.e. joint action versus execution blocks and joint action versus observation blocks) revealed significant differences in the dGCMs originating from some left BA 44 voxels to voxels of the bilateral cerebellum: values were significantly larger during joint action blocks compared to execution blocks (Fig. 3C & Table 5). This suggests that the directed influence of left BA 44 on bilateral cerebellum was significantly stronger during joint actions than during execution. Similar direct comparison of dGCMs between joint action and observation blocks did not reveal any significant difference.

Table 1. The directed influence of the source ROI 1 (BA 44) on the target regions in the joint action condition revealed with GCM. * The network that the target is part of. Two networks were identified in a previous study (Kokal et al., 2009): the putative mirror neuron system (pMNS) and integration network (int. network).

Source	Target	Network*	Hem	x	y	z	size(vx)
BA 44 (ROI 1)	SI / BA2	pMNS	L	-36	-35	48	10
	SI / BA2	pMNS	R	40	-33	63	13
	c. vermis	int. network	L	-3	-39	-6	33
	cerebellum	int. network	R	21	-66	-15	30
	thalamus	int. network	L	-6	-18	18	18
	MOG	int. network	R	39	-84	12	30

Table 2. The directed influence of the source ROI 2 (BA 6) on the target regions in the joint action condition revealed with GCM

Source	Target	Network	Hem	x	y	z	size(vx)
BA 6 (ROI 2)	c. vermis	int.network	L	-3	-39	-6	26

Table 3. The directed influence of the source ROI 1 (BA 44) on the target regions in the execution condition revealed with GCM.

Source	Target	Network	Hem	x	y	z	size(vx)
BA 44 (ROI 1)	MOG	int. network	R	36	-81	9	17

Table 4. The directed influence of the source ROI 1 (BA 44) on the target regions in the observation condition revealed with GCM.

Source	Target	Network	Hem	x	y	z	size(vx)
BA 44 (ROI 1)	c. vermis	int. network	R	3	-45	-3	33
	c. vermis	int. network	R	3	-72	-9	33
	MOG	int. network	L	-36	-87	3	23

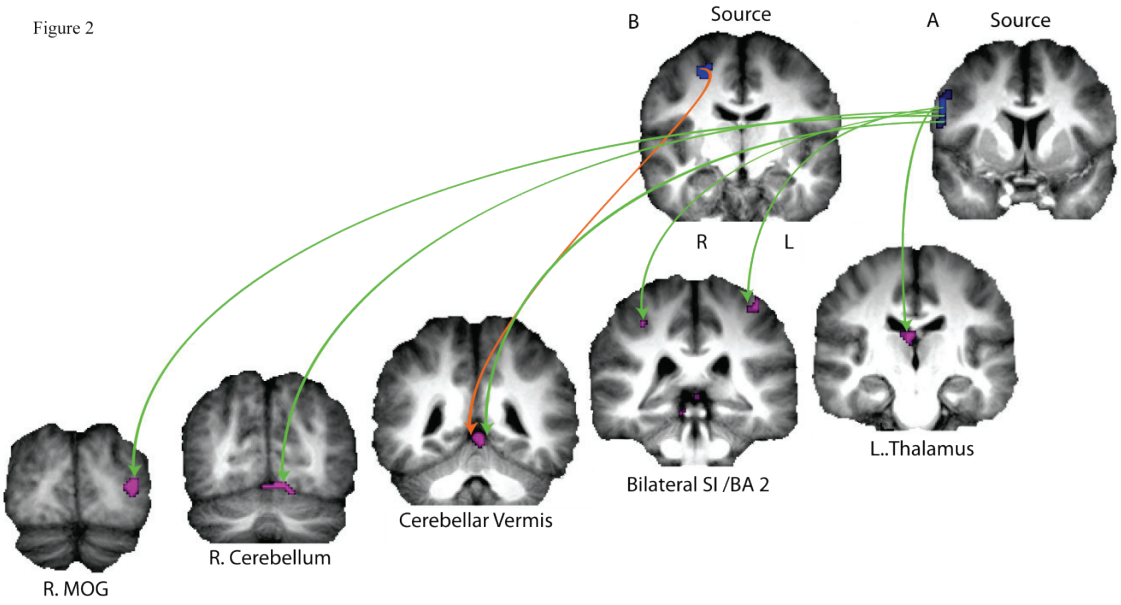
Table 5. The difference in directed influence of the source ROI 1 (BA 44) on the target regions between the joint action and execution conditions (joint action>execution) revealed with GCM.

Source	Target	Network	Hem	x	y	z	size(vx)
BA 44 (ROI 1)	cerebellum	int. network	R	9	-69	-18	19
	cerebellum	int. network	L	-3	-69	-15	13

Table 6. Source Regions of Interests for the GCM.

Source ROI	Area (Anatomy)	Area (BA)	Network	Hem	x	y	z	size(vx)
ROI 1	IFG	BA 44	pMNS	L	-58	8	26	26
ROI 2	preCG	BA 6	pMNS	L	-26	-10	52	22

Figure 2: The directed influence of the **(A)** source region BA 44 (blue) and **(B)** source region BA6 (blue) on the target regions (purple) in the joint action condition.The yellow **(A)** and orange **(B)** lines represent the information flow from source regions to the target regions.



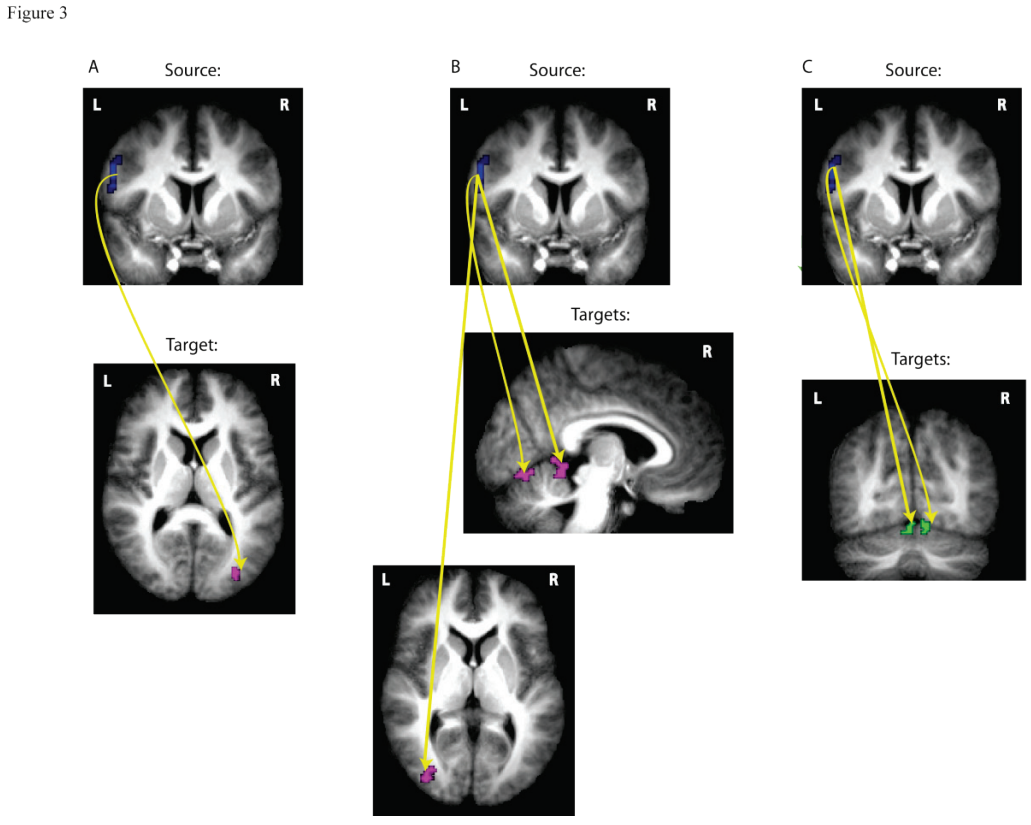


Figure 3: The directed influence of the source region BA 44 (blue) on the target regions (purple) in the execution **(A)** and observation **(B)** conditions. **(C)** The difference in directed influence of the source regions BA 44 (blue) on the target regions (green) between the joint action and execution conditions (joint action>execution). The yellow lines represent the information flow from source regions to the target regions.

3.4. Discussion

In our previous fMRI study, in contrast with other studies and theoretical accounts suggesting a central role for the pMNS for action integration in joint actions (Newman-Norlund et al., 2008; Newman-Norlund et al., 2007b; Sebanz et al., 2006b), we previously showed that the brain areas responsible for integration during joint actions fall outside the pMNS, especially in the anterior sites of the pMNS (the inferior frontal gyrus (BA 44) and precentral gyrus (BA 6)) (Kokal et al., 2009).

In the present study, we further explored the contribution of the pMNS in joint actions with a different method: GCM. We tested our hypothesis, formulated previously, that the anterior sites of the pMNS may not participate in integration directly, but do so indirectly by transforming observed and executed actions into a common code

(Etzel et al., 2008; Gazzola and Keysers, 2009; Kokal et al., 2009) and feeding this information to other brain regions that can then integrate the commonly coded action representations depending on the goal of a particular trial (Kokal et al., 2009). More specifically, we thought that Hebbian associations occur in the pMNS between performing a certain action and seeing and feeling that action (Del Giudice et al., 2009; Keysers and Perrett, 2004): While the participant saw himself perform certain actions in the past, Hebbian learning would have strengthened synaptic connections between neurons in the visual cortex that respond to the sight of his action, neurons in BA2 that represent proprioceptive information from the moving limb, and neurons in BA 6 and 44 that triggered the action. Because of the bidirectional nature of the connections between these regions (Keysers and Perrett, 2004), such connections would be strengthened both in the motor to visual and somatosensory and in the visual and somatosensory to motor direction. During action observation, seeing someone else perform a similar action would then trigger activity in BA2, BA 6 and BA 44 neurons involved in performing a similar action due to the visual similarity with our own movement triggering, through these strengthened synaptic, those premotor and somatosensory neurons which activity was associated with that of the visual neuron in past performances of the same action. At the same time, during motor execution, these strengthened synaptic connections would trigger activity in BA2 and visual neurons representing the visual and proprioceptive consequences of our own movements.

Simple reaction time experiments (Adam and Van Veggel, 1991; Michie et al., 1976) shows that it takes humans between 200 and 300ms to process the simplest visual stimuli and generate a simple motor response to that stimulus. Because, when we perform an action, it therefore also takes 200-300ms for the chain of event that could cause Hebbian learning (motor activity in BA 6/44 $\rightarrow$ overt movement of the arm $\rightarrow$ activity in the retina and peripheral somatosensors $\rightarrow$ activity in the visual and somatosensory cortices $\rightarrow$ synaptic input back to BA 6/44) and these Hebbian associations will develop predictive properties. For instance, while reaching to slide an object aside, by the time the visual cortex is representing the reaching movement and BA2 responds to the proprioceptive feelings of the arm reaching, the premotor cortices (BA 6 and 44) will already trigger the sliding phase of the movement that follows reaching after 200-300ms. Accordingly, Hebbian associations will strengthen

synapses between seeing (visual cortex) and feeling (BA2) a movement and programming the next movement (BA 6 and 44) that normally follows the first movement after 200-300ms. While seeing the actions of others, our brain would still take 200-300ms to respond to its perception of the actions of others (as in any reaction time task) but the neural representation of the actions of others in BA 6/44 would be a representation of the actions most likely to occur in 200-300ms. The motor reaction time and predictive horizon would then precisely cancel each other out, and the brain could actually act in synchrony with others instead of lagging behind.

Through this set of associations, seeing the actions of others will trigger expected somatosensory and motor representations, and vice versa, programming one's own actions would trigger visual and somatosensory representations. Viewing the actions of others and performing one's own actions would therefore be associated with the same type of representations in motor, somatosensory and visual representations. Brain regions that represent a particular goal to be achieved with a partner (i.e. creating an angle or straight line in our experiment) need to coordinate the participant's own actions with what he sees another individual perform. This task would become computationally more difficult, if the participants' own actions were represented in a different code than those of the observed agent, and simpler, if they were represented in the same code. The pMNS could therefore facilitate the role of such integrative brain regions by doing what it seems to do: representing the participant's and the experimenter's (anticipated) actions in the same code (Etzel et al., 2008; Keysers et al., 2003).

Here we show that during joint actions, anterior sites of the pMNS in the left hemisphere (BA 44 and dorsal BA 6) indeed were exchanging information with the integration network during joint actions: GCM showed that left BA 44 sent significantly more information to than it received from the integration network (right MOG, left thalamus, left cerebellar vermis and right cerebellum). In addition, left BA 6 exchanged information with the cerebral vermis by sending significantly more information than receiving from it. Thus, the anterior sites of the pMNS could play a role in the integration of actions during joint actions by feeding information into the areas that are part of the integration network suggesting that these two anatomically separate networks (the pMNS and integration network) work in concert during joint actions.

In addition, our analysis showed that during joint actions the anterior sites of the pMNS also sent information to BA2 within SI which was part of our pMNS network, because it was active both during the solo observation and execution of the actions in our task (Kokal et al., 2009). Although single cell recordings in BA2 have so far not systematically explored the presence of mirror neurons, reviews of the literature (Caspers et al.; Keysers et al., 2010) provide strong evidence for the fact that BA2 is systematically activated while we perform and observe the actions of others. This suggests that the pMNS is constituted of two branches: the classic motor branch and a less explored somatosensory branch that represents the proprioceptive and tactile input one would experience when performing similar actions (Keysers et al., 2010). The information flow we found here between BA 44 and BA2 therefore suggests that these two branches interact during joint actions, with the motor branch

possibly triggering representations of the expected somatosensory consequences of the observed and/or planned actions.

Apart from providing empirical evidence for information exchange within the pMNS and between the pMNS and integration network in the service of joint actions, our results also revealed the predominant direction of the underlying effective connections: the information flow was predominantly backwards (i.e. from frontal left BA 44 to more posterior areas: bilateral BA2, right MOG). Recent simulations performed by Schippers and colleagues (manuscript in preparation) suggest that even in the presence of variability in hemodynamic response latency between different brain regions, the detected direction of prevalent information flow detected using differential GCM within a condition correctly identifies the true direction of information flow in >80% of the cases. Another study using simulations demonstrated that GC could be used to infer neuronal causality reliably (accuracies up to 90%) in the presence of neuronal delays (Deshpande et al., 2010). We will, therefore, discuss how the backwards information flow detected in our study is compatible with the increasingly prominent concept of generative/forward models (Gazzola and Keysers, 2009; Keysers and Perrett, 2004; Kilner et al., 2007; Kilner et al., 2004; Miall, 2003; Wolpert et al., 2003; Wolpert et al., 1995; Wolpert and Miall, 1996).

It has been proposed that while the forward connections from visual to premotor regions form inverse models through which the visual information is converted to predicted motor plan; the backwards connections, from premotor to visual and somatosensory regions generate the predicted sensory outcome of the action representations triggered in premotor regions, forming forward (generative) models (Gazzola and Keysers, 2009; Iacoboni et al., 2001; Jabbi and Keysers, 2008; Keysers and Perrett, 2004; Kilner et al., 2007; Kilner et al., 2004; Luppino et al., 1999; Miall, 2003; Wolpert et al., 2003; Wolpert et al., 1995; Wolpert and Miall, 1996). In this concept, the premotor cortex is part of both forward and inverse models (Fig. 1C) and closes a loop of information flow circling between premotor, somatosensory and visual areas which could play a key role in social actions (Demiris, 2002; Gazzola and Keysers, 2009; Kilner et al., 2007; Schaal et al., 2003; Wolpert et al., 2003), particularly in the case of joint actions requiring tight temporal synchrony between cooperative partners. As mentioned above, based on simple reaction time experiments, it takes us about 200-300ms to respond to a stimulus. Accordingly, instead of being synchronized with the actions of others, our actions would lag several hundreds of milliseconds behind the perceived actions of our partner. However, humans can do much better than that. In the well-studied case of music (Keller, 2008), it has become apparent that two musicians can synchronize their performance to each other's timing with asynchronies of ~30ms (Keller et al., 2007), which is also the threshold at which humans typically perceive two notes as asynchronous (Szymaszek et al., 2006). Although an example of auditory-motor rather than visio-motor synchrony, joint music playing shows that the brain can overcome sensory-motor delays to reduce inter-individual asynchronies below the perceptual threshold. The fact that people actually tap slightly ahead of a beat they should synchronize with (Dunlap, 1910; Johnson, 1898; Miyake, 1902; Repp, 2005), suggests that predictions probably play a role, and the fact that musicians are better at synchronizing with prerecorded pieces they played themselves supports the idea that motor simulation, as

described in our Hebbian learning scenario above, could play a role (Keller et al., 2007). Accordingly, it has been proposed that one way to be able to synchronize one's actions with others or external stimuli would be to base our motor planning not on actual (and therefore delayed) sensory input, but on the prediction of forthcoming actions, as provided by generative/forward models (Gazzola and Keysers, 2009; Kilner et al., 2007; Kokal et al., 2009; Wolpert et al., 2003; Wolpert and Ghahramani, 2000; Wolpert et al., 1995; Wolpert and Miall, 1996). However, so far, empirical evidence for such generative models in joint action experiments remains scarce.

In our experimental design, each trial was composed of an unpredictable beginning and a more predictable continuation. At the commencement of each trial, the participant needed to detect the side the experimenter decided to move her part of the device towards. This phase was relatively short (<500 ms). Thereafter, the participant could predict how the movement of the experimenter would continue in the remaining 1.5 s, and s/he only needed to adjust her/his own actions to this predictable trajectory. In this context, generative models predict the predominant direction of information flow that should occur in the brain. Only in the initial 0.5 s should information flow predominate in the 'forward', visual to premotor direction because predictions cannot yet be formed accurately. During the longer remaining time (~1.5 s), predictions can be formed, and information flow in the 'backwards', frontal to visual and somatosensory direction should build up. Given that these 'backward' flowing predictions are known to cancel the neural representation of expected visual information from the visual cortex (Hietanen and Perrett, 1993; Hietanen and Perrett, 1996) and expected somatosensory information from the somatosensory cortex (Blakemore et al., 2000), the forward information flow in the visual to frontal and somatosensory to frontal direction should be much reduced. Overall, integrating these predictions over the entire duration of the trial, information flow in the backwards, premotor to visual and somatosensory direction should therefore prevail. The fact that this is exactly what we measured in our experiment provides support for the notion that the pMNS is part of forward/generative neural model (Gazzola and Keysers, 2009; Keysers and Perrett, 2004; Kilner et al., 2007; Wolpert et al., 2003) that could play a key role in joint actions not only by transforming observed and executed actions in a common code but also by computing predictions that can overcome otherwise inevitable neural delays.

In addition to the predominantly 'backwards' cortical information flow we also found that both left BA 44 and BA 6 sent more information to the cerebellum and cerebellar vermis, than they received from it, respectively. These regions of the cerebellum play important roles in motor control and are thought to be part of the forward models central to every form of skilled motor control (Blakemore et al., 2001; Blakemore and Sirigu, 2003; Dum and Strick, 2003; Kawato et al., 2003; Stein and Glickstein, 1992; Wolpert and Miall, 1996). During motor control, the convergence of input from the premotor cortex and sensory structures makes the cerebellum an ideal site for calculating in real time the error between intended and actual movement, and using this error to improve motor performance (Wolpert et al., 1998). These real time calculations seem to be important for the actions performed by individuals in solo conditions (Wolpert and Ghahramani, 2000). One might speculate, that during joint actions, the cerebellum may play a similar integrative role in detecting errors in

synchrony between one's own actions and those of others. The fact that the cerebellum receives more input from the premotor cortex during joint actions compared to solo motor execution suggests that during joint actions, the cerebellum might receive information about the (predicted) actions of the other agent in addition to the intended motor command that the cerebellum is known to receive from premotor cortices during solo action execution. This would provide the cerebellum with the information it would need to fine tune the way in which the actions of the two agents need to be coordinated to achieve their common goal.

At first sight, one might however wonder why we failed to find any brain region that primarily sends information to the frontal pMNS regions. After all, these regions have to receive visual information about the actions of the partner from somewhere. It is important to keep in mind however that GCM analyses of fMRI data employ a *differential* Granger approach (Roebroeck et al., 2005). Simulations have shown that GCM applied to fMRI signals cannot accurately infer whether information is sent from one region to another per se, however it can establish whether *more* information is sent from one region to another than vice versa (Roebroeck et al., 2005). By following that approach, our analyses showed that during joint actions, information flow is *more* pronounced in the premotor to somatosensory direction than vice versa. Our analyses therefore do not show that the frontal pMNS regions do not receive information from more posterior regions, nor that there is no information flow between regions where our analysis find no significant differential GC - however that more information is sent in the backwards direction, as expected by generative models. Testing the concept of a loop of information would need data of higher temporal resolution to separate the first couple of hundreds of ms from the rest of the trial. Thus, in the future, we plan to use methods with higher temporal resolution (EEG or MEG) in order to investigate interactions at a time scale closer to that of the neural processing itself and to explore the prediction that the predominant direction of influence shifts between the unpredictable beginning and the predictable continuation of each trial.

It had been suggested that because various brain regions can differ in their hemodynamic response function, and Granger causality is based on temporal precedence, differential Granger causality (dGC) might indicate information flows from A→B simply because region A has a faster hemodynamic response than region B (Roebroeck et al., 2005). To avoid such biases, Roebroeck and colleagues suggested to look at dGC in different conditions, and to focus on dGC results that are present in one but absent in another condition (Roebroeck et al., 2005). Directly contrasting dGC between two conditions was not performed in their paper. Using such a conservative approach instead of interpreting all significant dGC results obtained from our joint action blocks, the main message of our paper remains unchanged. The anterior pMNS regions evidenced significant positive dGC values with BA2 during the joint action condition but not the solo conditions, providing further evidence for information flow in the anterior to posterior direction within the pMNS during joint actions. There was also an increased dGC from anterior pMNS to the cerebellum during joint actions compared to solo motor execution, providing further evidence for the interaction between the pMNS and the integration network in our task. This suggests that the information transfer within the pMNS and between the pMNS and the integration

network is indeed specific for cases in which participants need to coordinate their own actions to external stimuli, such as was the case during joint actions. Our own data simulations , performed by Schippers and colleagues (2011), using realistic differences in hemodynamic response functions and a group analysis approach, however suggest that the direction of predominant information flow derived from a single condition is accurate in over 80% of the cases suggesting that the results of the analysis in the joint action condition alone can be interpreted more safely than Roebroeck and colleagues had suggested (Roebroeck et al., 2005; Schippers et al., 2011).

In summary, we present evidence that there is information flow from the anterior sites of the pMNS to the integration network, i.e. the bilateral cerebellum and maybe (if single condition dGC can indeed be interpreted safely as suggested by Deshpande et al. (2010) and Schippers et al., in preparation) right MOG, left thalamus and left cerebellar vermis, and posterior sites of the pMNS, i.e. BA2. This sheds new light onto the role the pMNS during joint actions. As suggested by our previously published traditional analysis of this data, the pMNS does not seem to be directly involved in the task dependent integration of observed and executed actions during joint actions (Kokal et al., 2009). However, the pMNS could contribute to joint actions indirectly, by transforming observed and executed actions into a common code and being part of a generative model that could predict the future somatosensory and visual consequences of observed and executed actions in order to overcome neuronal delays. This information is then sent to regions such as the cerebellum that can integrate our own actions with those of others and permit the exquisite temporal coordination characterizing so many joint actions.

Supplementary Information

Table S1. Abbreviations used in the paper together with their meaning.

ang	angle joint action condition
BA44	Brodmann area 44
BA6	Brodmann area 6
BOLD	blood-oxygen-level dependent
EPI	echo-planer imaging
exe	execution condition
fMRI	functional magnetic resonance imaging
GCM	Granger causality mapping
GLM	general linear model
Hem	hemisphere
IFG	inferiror frontal gyrus
IPL	inferior parietal lobule
MOG	middle occipital gyrus
MTG	middle temporal gyrus
obs	observation condition
PF	parietal area F
pMNS	putative mirror neuron system, i.e. obs>0 AND exe>0
preCG	precentral gyrus
RL	red light
ROI	region of interest
SB	start button
SI	primary somatosensory area
SII	secondary somatosensory area
SPL	superior parietal lobule
str	straight joint action condition
Vox	voxel

4. Synchronized Drumming Enhances Activity in the Caudate and Facilitates Prosocial Commitment - If the Rhythm Comes Easy

Under Review as: Kokal I, Engel, A., Kirschner, S., Keysers, C. (resubmitted after revisions): Synchronized Drumming Enhances Activity in the Caudate and Facilitates Prosocial Commitment - If the Rhythm Comes Easy.

ABSTRACT

Moving a set dinner table often takes two people, and doing so without spilling the glasses requires the close coordination of the two agents' actions. It has been argued that the mirror neuron system may be the key neural locus of such coordination. Instead, here we show that such coordination recruits two separable sets of areas: one that could translate between motor and visual codes and one that could integrate these information to achieve common goals. The former includes regions of the putative mirror neuron system, the latter, regions of the prefrontal, posterior parietal and temporal lobe adjacent to the putative mirror neuron system. Both networks were more active while participants cooperated with a human agent, responding to their actions, compared to a computer that did not, evidencing their social dimension. This finding shows that although the putative mirror neuron system can play a critical role in joint actions by translating both agents' actions into a common code, the flexible remapping of our own actions with those of others required during joint actions seems to be performed outside of the putative mirror neuron system. Why does chanting, drumming or dancing together make people feel united? Here we investigate the neural mechanisms underlying interpersonal synchrony and its subsequent effects on affiliation among synchronized individuals. We hypothesized that reward areas in the brain would be active when individuals experience synchrony during drumming action, and that these reward signals would facilitate prosocial commitment among drum partners. 18 female non-musicians were scanned with functional magnetic resonance imaging while they drummed a rhythm, in alternating blocks, with two experimenters: one drumming in-synchrony and the other drumming out-of-synchrony relative to the participant. During the last (manipulation) run, one experimenter drummed continuously with half of the participants in- and with the other half out-of-synchrony. After scanning, this female experimenter 'accidentally' dropped eight pencils, and the number of pencils collected by the participant was used as a measure of prosocial commitment. Results revealed that participants who mastered the novel rhythm easily before scanning showed increased activity during synchronous drumming in a brain area (caudate) that also responded to monetary reward in the same participants. The activity in the caudate during experienced synchronous drumming also predicted the number of pencils the participants later collected to help the synchronous experimenter of the manipulation run. In addition, participants collected more pencils to help the experimenter when she drummed in synchrony in the manipulation run compared to asynchronously. By showing an

overlap in activated areas during synchronized drumming and monetary reward, our findings suggest that interpersonal synchrony triggers the brain's reward system.

4.1. Introduction

Humans are the only primates that spontaneously synchronize their voices and movements during music making and dancing (Fitch, 2006), a behavior found across all cultures (Wallin, 2000) and emerging early in human childhood (Kirschner and Tomasello, 2009). One hypothesis claims that music and dance are culturally evolved tools for fostering group cohesion and commitment, thereby increasing prosocial in-group behavior and cooperation (Huron, 2001; McNeil, 1995; Roederer, 1984). In fact, within a study comparing four different experimental groups of male adults, (Anshel and Kipper, 1988) showed that the group, who was singing together, cooperated better in a prisoner's dilemma game and scored higher on a questionnaire on trust, than the groups that either read collectively a poetry, listened to music or, watched a film together. Likewise, (Wiltermuth and Heath, 2009) demonstrated increased cooperation among students after joint singing, compared to no singing or forced "asynchronous" singing along with a song played from headphones at different individual tempi. Similarly, (Hove and Risen, 2009) found that the degree of synchrony in a finger-tapping task between participant and experimenter correlates with subsequent affiliation ratings. Finally, (Kirschner and Tomasello, in press) showed that joint music making facilitates prosocial and cooperative behaviors already among four-year-old children.

Although interpersonal synchrony seems to be universally important, little is known about the neural basis of the phenomenon. Therefore, we asked, how the prosocial effects of synchronized interpersonal activity are mediated by the human brain. For changing prosocial behavior after interpersonal synchrony, three sub-phenomena must occur: (i) individuals must be capable of synchronizing each other's activity, (ii) they should share the motivation to do so, for instance because it feels rewarding, and (iii) their prosocial tendencies should be sensitive to synchronized behavior. If any brain structure were common to these three sub-processes, it would form an ideal candidate structure for linking synchronized activity to prosocial behavior. As we will see below, the caudate nucleus seems to be involved in all three sub-processes, i.e. the capacity to synchronize with others, reward based processes and modulation of prosocial behavior and will therefore be at the core of our investigation.

First, studies investigating how we can synchronize our actions to external stimuli found that, among others, the basal ganglia, which include the striatum (caudate and putamen), the pallidum and the substantia nigra, are important for our *capacity* to synchronize our actions to external stimuli (Lewis et al., 2004; Rao et al., 1997; Repp, 2005; Wing, 2002). Second, neuro-economic studies looking at reward areas during decision making have shown that the striatum is activated by stimuli associated with both monetary (Izuma et al., 2008; Knutson et al., 2001; Saxe and Haushofer, 2008; Zink et al., 2008) as well as social rewards such as a gain in reputation (Izuma et al., 2008). Third, studies investigated the neurobiology of

prosocial behavior using economic exchange tasks to manipulate trust and social risk taking (Baumgartner et al., 2008; Delgado et al., 2005; Delgado et al., 2004; King-Casas et al., 2005) have shown that the striatum and, in particular the caudate, also play an important role in facilitating prosocial behavior (King-Casas et al., 2005). Finally, an accumulating body of research suggests that the striatum is involved in adapting future behavior based on reward based decision making (O'Doherty, 2004; Schonberg et al., 2007; Tricomi et al., 2004) and reinforcement learning (Balleine and O'Doherty, 2010; White, 2009). Within the striatum, the caudate seems to be particularly sensitive to the contingency between an action or stimulus and their positive and negative consequences (Tricomi et al., 2004), thereby modulating future behavior based on reward history (Montague and Berns, 2002): lesions to the caudate in animals were found to impair stimulus-response learning, i.e., prevent animals from appropriately changing their response to a stimulus as a function of past rewarding experience with that stimulus (see (White, 2009) for a review).

In summary, the caudate within the striatum is at the intersection of a number of important sub-processes that *could* link synchronized activity to feeling of reward and future prosocial behavior. In this study we directly test this possibility. We investigated how experiencing synchrony during rhythmic musical actions is processed within the human brain in general and the caudate in particular and how this modulates prosocial behavior at a later point in time. Based on the role of the caudate in generating synchrony and in reward processing, we hypothesized that synchrony during joint drumming triggers activity in reward processing regions of the brain, particularly the caudate. Based on the role of the caudate in reward based stimulus-response learning and prosocial behavior, we hypothesized that the activity in the caudate during joint drumming leads to a change of the association between the stimulus of the drum partner and future prosocial behavior.

Finally, we may all experience that if singing a song takes all our concentration, because we struggle to remember the lyrics, singing it with others is not particularly rewarding or binding. If we sing it easily and confidently however, chanting it together becomes a thrill. Accordingly, we further hypothesized that the effect of synchrony on the caudate and prosocial behavior correlates with the ease with which participants can acquire the drumming task.

4.2. Methods

Participants: 18 healthy volunteers (all right-handed and female; mean age 23 years ranging 19-30 years) with normal or corrected to normal vision and without a history of neurological, major medical, or psychiatric disorders participated in the present study. Two participants of the initially 20 recruited participants were excluded from the study. These two participants reported at the end of the scanning that they suspected having not really drummed with the experimenters during scanning, undermining the social relevance of the manipulation. Only females were recruited in order to avoid possible gender confounds since the main experimenter who performed the prosocial commitment test (see below) was always the same female. None of the volunteers had any musical training or had ever played a musical instrument (except music classes at primary school). Participants gave their written informed consent and

were paid for their participation. The experiment was approved by the Medical Ethical Commission of the University Medical Center Groningen, the Netherlands.

Experimental procedure: All participants performed: 1) a training session in which the participants were familiarized with a syncopated rhythm and their drumming task. Unknown to the participants, their performance was evaluated and rated as 'ease of rhythm imitation' during this session; 2) an fMRI scanning session with a) an fMRI localizer involving a monetary reward task to functionally define the sectors of the caudate involved in reward processing; b) an fMRI session consisting of 2 runs in which the participants believed that they would drum with one of the experimenter in half of the blocks and with the other experimenter in the other half. With the aim to manipulate the experienced synchrony of the participant and the co-drummers, one co-drummer was in- (synch) and the other out-of-synchrony (asynch); c) a manipulation run in which participants believed that they would drum together with the main experimenter (she either drummed in- or out-of-synchrony with the participant); 3) a prosocial commitment test, immediately after the manipulation run, to assess the propensity to help the main experimenter (we call the experimenter who performed the helping test main experimenter; see Fig. S1A&B).

Training: Before scanning, participants were familiarized with a syncopated rhythm consisting of 10 notes (Fig. S1A) and learned to drum the rhythm by using a button box. The rhythm had to be played with the two index fingers of two hands, starting with the left finger, followed after 600 ms by two right finger beats, one left and one right finger beat (each 300 ms long). After 900 ms, two left finger and two right finger beats (each 300 ms long) were followed by a last left finger beat (c.f., Fig. S1A for score and timing). The rhythm was introduced by a demonstration video presenting the rhythm two times successively performed by a male experienced drummer with bi-manual index fingers on African bongos (Supporting Information Video S1, 10s long). In this video only the trunk, arms and hands of a male person and a bongo on a table in front of the actor was visible. The person in the video was not any of the experimenters. After the demonstrator played the same rhythm two times, the video stopped (10 s). Each participant watched this video two times unless the participant asked for more repetitions. Participants were informed they could try to reproduce the rhythm using the left- and right-most button of an MRI compatible box, while watching the demonstration videos. Later they practiced the rhythm with the computer presentation program and the button box; the left- and right-most buttons were associated with two different prerecorded bongo sounds. The trial structure of the training trials was identical to that of the experiment (see Fig. S1A).

During training, both experimenters rated the progress of the participants in acquiring the preset rhythm in order to quantify individual participant's 'ease of rhythm imitation'. Participants received a score ranging from 1 to 5 based on observations including the number of times the participant asked to watch the demonstration movies, whether she asked for additional help from the experimenter and how early she managed to reproduce the rhythm (see Supporting Information Table S1 for the detailed rating definition).

After the individual training, participants practiced with the experimenters. The participant and one experimenter sat next to each other. Participants used the button box (2 buttons) and the experimenter used a keyboard (2 buttons), both mounted to the

presentation computer. The computer presentation program presented four different sounds upon a button press of these four buttons (experimenter's button presses were associated with deeper tones than the participants' (Supporting Information Listening Examples S1 and S2). Participants played the rhythm with a co-drumming experimenter for three consecutive blocks (3x8 repetitions) and later with the other experimenter for three consecutive blocks. As the experimental manipulation, for half of the participants the main experimenter drummed in synchrony with the participant (note that the experimenter was able to see the participant's hands and button box since they sat side by side; c.f. Supporting Information Listening Example S1), whereas the other experimenter drummed in asynchrony with the participant (by delaying or preceding her button presses) on purpose (c.f., Supporting Information Listening Example S2). For the other half of the participants, the role of the experimenters was reversed: the main experimenter drummed out of synchrony with the participant and the other experimenter drummed in synchrony with the participant. One of the experimenter was wearing a red t-shirt and the other experimenter a blue t-shirt. This was used to give a color cue during scanning in order to inform participants with whom they would drum. This last part of the training was not used for the 'ease of rhythm imitation' rating in order to separate social factors studied later in the experiment from people's individual aptitude, as evaluated by this score.

Scanning environment: A 3T Philips scanner was used and a 'soft-tone' option was set on for the gradient noise to interfere less with hearing the drums. During scanning, supine participants saw through a mirror on the top of the head coil the visual instructions projected via an LCD projector. All participants wore MRI-compatible headphones (MR confon GmbH, Magdeburg, Germany) without earplugs. A conventional MRI-compatible response box (fORP, Current Designs, Inc., Philadelphia, USA) with 4 buttons was placed in front of the participants on a table so that they could use the box bimanually. The first and fourth (the left-most - red and the right-most - blue) buttons were used as bongos during the experiment (see Fig. S1A); the second, third and fourth buttons (from left) were used during the localizer experiment. All Stimuli were programmed and presented using the software Presentation 12.0 (Neurobehavioral systems, Davis, CA, USA).

Localizer Experiment: The participants performed a simple gambling task during scanning (Fig. S1C) in which their earnings from a randomly picked run would be given to them at the end of the experiment. Thus, they were asked to try to earn as much money as possible. This task was adapted from the monetary reward task generously provided by Izuma and colleagues (Izuma et al., 2008). Since Izuma and his colleagues have shown in a previous experiment, that a monetary and a social reward activate very similar brain structures, we used the same monetary reward task in order to identify the brain areas related to reward in our participants (Izuma et al., 2008).

In each trial (3 s), the participants saw three cards with labels ''A'', ''B'' and ''C'' side by side, all three cards were presented in the choice period (2 s). Then they were asked to choose one card by pressing the spatially corresponding button of their response box (using the right index, middle, or ring fingers). After the response, they saw the chosen card highlighted with a white border and the outcome (1 s). If the

subject did not press any button (i.e., choose a card) within 2 s, the card they had chosen in the previous trial was automatically chosen, and its outcome was displayed.

Blocks were constituted of 8 trials and lasted 24 s. Two types of blocks – reward and non-reward blocks - were distinguishable for the participant by the color of the font on the screen. In the monetary reward blocks, the outcome of choosing a particular card was randomly associated with 0, 0.30 or 0.60 EUR, and the amount was shown on the screen. In the no reward blocks (NMR), the outcome was always ‘‘XXX’’, indicating no reward. Additionally there were baseline blocks during which a red cross was presented. For half of the subjects, the color of the letters on the cards used for the reward and non-reward trials was red and blue, respectively, while for the other half of the participants the color assignment was switched.

Unknown to the participants, the total amount one could earn in each monetary reward block was predetermined and defined as a high and a low reward condition: In the high monetary reward blocks (HMR), participants earned on average 3.3 EUR each (range = 2.7–3.9 EUR), which was consistently higher than the expected value of eight reward trials (2.4 EUR). In the low monetary reward (LMR) blocks, they earned an average of 1.5 EUR each (range = 0.9–2.1 EUR), which was consistently lower than the expected value. Two reward blocks were always separated by a NMR block or a rest block (a red cross). Thus the start and end of the reward manipulations could be clearly defined. The localizer experiment comprised 4 runs (each run had each five blocks of HMR, LMR, NMR and baseline) and lasted 8 min.

Drumming Experiment: The task of the participants was to play the rhythm that they practiced in the training as correctly as possible. They were explained that the two experimenters, one wearing a red, the other a blue T-shirt, both sitting in the control room, would drum with them in real time in alternating blocks as in the last part of the training. A colored square on the T-shirt of the drummer in the demonstration video indicated with whom of the experimenter they would drum. However, in order to standardize our experimental conditions, the co-drumming in each trial was computer simulated during the experiment. Importantly, participants were not instructed or encouraged either to drum in synchrony with the experimenters or to attend the drums of the co-drummer.

Each block during scanning started with a demonstration video (10 s, Supporting Information Video S1, described in detail in the *Training* section) followed by 8 trials. 300 ms after the end of the video, the numbers ‘‘3’’, ‘‘2’’ and ‘‘1’’ appeared on the screen, indicating the pulse of the rhythm. Each number was presented for 300 ms and 300 ms of black screen was inserted in between numbers. Participants were instructed to start playing their drums whenever they saw the number ‘‘1’’ on the screen (appearing 1500 ms after the end of the video). In order to help participants to keep the beat across repetitions of the rhythm, they saw the number ‘‘3’’ on the screen when they had to play the last note of the rhythm, followed by 300 ms of black screen, 300 ms of “4”, and 300 ms of black screen to ensure a total of 900 ms of silence between repetitions of the rhythm. After that, the new trial started with the presentation of number ‘‘1’’ (300 ms) to cue a new instance of the rhythm (see Fig. S1A for the time course of a trial). These numbers served as indications for beats of a 4/4 bar at the tempo 100 beats per minute. Participants learned to use these visual instructions in the training section and were told that the co-drumming

experimenter would also use these visual instructions. Blocks within the experiments comprised two different conditions:

1) Synchronous Drumming (synch) Block: Participants played 8 trials of the rhythm and were lead to believe that they did so together with the experimenter they had experienced as synchronous during the training before scanning. In reality, the presentation program was used to simulate the synchronous experimenter by presenting the correct note after a randomized 15-75 ms interval following the button press of the participant (Supporting Information Listening Example S1). This was done to simulate a synchronous drummer adapting his/her beat to that of the participant within a tight but varying time window creating a natural synchronous drumming. Using only positive time delays relative to the participant ensured that the participant could not entrain to the experimenter.

2) Out of Synchrony Drumming (asynch) Block: Participants played 8 trials of the rhythm and were lead to believe that they drummed together with the co-drumming experimenter who was not in synchrony with the participants during the pre-training. In reality, the presentation program presented different prerecorded rhythms randomly in this block (Supporting Information Listening Example S2). These prerecorded rhythms were composed by randomly shifting the timing of the original notes of the sequence (-400 to +300 ms). In piloting the experiment, this jitter was perceived as corresponding to a drummer unable to keep the beat while preserving the overall structure of the rhythm.

All blocks were separated by 14 ± 2 s random pauses (baseline) with a red cross presented in the center of the screen. In total, the experiment consisted of three runs. The first two runs lasted 16 minutes and each contained 4 *synch* and 4 *asynch* blocks in pseudo-random order counterbalanced between runs and participants. The last run was designed as a manipulation run: only the main experimenter (instead of alternating two experimenters) drummed with the participants for five blocks. She was the in-synch drummer for half and the out-of-synch drummer for the other half of the participants. Importantly, to ensure that the main experimenter is blind to the experimental condition for her to perform the prosocial commitment test (following this last, 'manipulation run') without experimenter bias, the other experimenter randomly picked a presentation program that simulated an in- or out-of-synch drummer (as described above). Thus, the main experimenter neither knew during the training nor during the following prosocial commitment test whether she had supposedly drummed synchronously or asynchronously in this last manipulation run. Naturally, this randomization led to 4 different possible histories: 2 role-switch configurations in which the main experimenter could be the synchronous experimenter during the training and the first 2 runs of the experiment but a asynchronous experimenter during the manipulation run or vice versa; 2 no-role switch possibilities in which the main experimenter was either the synchronous or asynchronous experimenter during the training, the first 2 runs of the experiment as well as in the manipulation run. We had 3 participants in each of the role-switched groups (initially, we had two more participants in the role switch groups, however two of those participants were excluded, see description *Participants*) and we had 6 participants in each no-role switch groups.

Prosocial Commitment Test: This test was performed to measure the prosocial commitment of the participants towards the main experimenter who had drummed - according to the experimental condition - either in- or out-of-synchrony with the participants in the manipulation run. The participants were not aware that this was a test and the main experimenter did not know if she were an in- or out-of-synch drumming partner relative to the participant during the manipulation run. Immediately after the end of scanning, participants were asked to fill out a questionnaire and were guided by the main experimenter to the waiting room. This room was empty except for one table standing at the side, thus the experimenter explained that she would leave to bring a chair and pencils so that the participant could sit down and fill out the questionnaire. After a minute, she came back, holding the chair with both hands and a plastic cup containing 8 pencils in one hand. The moment she entered the room, she pretended to accidentally drop the plastic cup, such that all eight pencils fell on the floor and the pencils spread around the room. The experimenter's hands were occupied carrying a chair when she dropped the pencils and it took her about 10 s to place the chair. Given that the distance between the various pencils and the participant varied considerably, in this 10s time window participants could decide how many pencils they would pick up to help the experimenter: none, only those within close reach, or even those requiring the participant to walk around to pick them up - leading to a relatively continuous dependent variable. As a measure of the participant's prosocial commitment towards the experimenter, we therefore counted the number of pencils that the participant picked up. After that, the participant filled out a questionnaire about the experiment. With this questionnaire we surveyed the perceived difficulty with the experiment and their enjoyment of the drumming task during the scanning (e.g., How much fun the participant had while playing with the experimenter wearing a blue t-shirt? 1-5 Likert scale, 5 = enjoyed a lot, questions can be found in the Supporting Information Table S2).

Behavioral Data Analysis

Drumming Performance during Scanning: We evaluated our non-musician participants' performance during scanning by analyzing the onsets of the participants recorded button presses.

fMRI Data Analysis

Data acquisition: Imaging was performed with a Philips Intera 3T Quaser with a synergy SENSE eight channel sense head coil and maximum gradient strength of 30 mT/m with a soft tone sequence. Head movements never exceeded 3mm in a run. We used a standard single shot EPI with TE = 27 ms, TA= 1.45 s, TR= 1.5 s. For each volume, 30 AC-PC aligned axial slices of 4 mm thickness, without slice gap and a 3.5 x 3.5 mm in plane resolution were acquired to cover the entire brain using an interleaved slice acquisition. A T1 weighted structural scan was acquired with TR = 9 ms, TE = 3.53 ms, flip angle= 8 deg.

Data preprocessing: We used SPM5 (www.fil.ion.ucl.ac.uk/spm) implemented in MATLAB 6.5 (Mathworks Inc., Sherborn, MA, USA) for fMRI data analysis. All EPI volumes were aligned to the first volume acquired for each participant and a mean EPI image was generated after realignment. Spatial normalization was performed by

co-registering the structural volume to the mean EPI, segmenting the co-registered structural image, determining the normalization parameters required to warp the gray matter segment onto the gray matter MNI template, and applying these parameters to all EPI and structural volumes. Normalized images were written with an isotropic resolution of 2 mm for EPI and 1mm for structural images. The normalized EPI images were smoothed with an 8 mm FWHM isotropic Gaussian kernel. The normalized structural images (T1) were then averaged across participants for visualization of results. The preprocessing of the experiment and the localizer task was done with same procedure and the same normalization parameters.

General data analyses: Functional data were analyzed using a general linear model (GLM) separately for each participant and voxel using SPM5. We modeled the data in a block design fashion. Each block consisted of 8 trials; in total each participant performed 8 blocks of 8 trials per condition (64 trials total). Although there were mistakes in some trials in the blocks, the number of trials with mistakes for all 8 blocks combined was very low (mean=2.11/64 trials in the *synch* condition; mean= 3.06/64 in the *asynch* condition; see Results, Behavioral Results). Given that on average 97- 95% of the trials were therefore without mistakes, we decided not to exclude any trials or blocks from the analysis. The localizer task was modeled in a separate design matrix in a block design fashion.

Single participant analyses: For the drumming experiment, the GLM was performed using separate predictors for the conditions *synch*, *asynch* and the video (demonstration video, which was shown in the beginning of each block). Likewise, for the localizer task, the GLM was performed for the HMR, LMR and NMR predictors in a separate design matrix. Each predictor was a boxcar function that reflected the length of the block. The boxcar functions were convolved with the hemodynamic response function, and fitted separately for each run to the data. In addition, the head motion and rotation along the three axes were entered as 6 covariates of no interest in the design matrix to single out motion artifacts although motion never exceeded 3 mm within a run.

Population analyses: At the second level of analysis, the contrast images from the single level analyses were entered into random-effects models (RFX) to make inferences at a population level. Group analyses were thresholded at the voxel-level at $p < 0.005$ (uncorrected). To control the overall rate of false positives, only results also surviving a False Discovery Rate correction (FDR) of $p<0.05$ are reported. This double procedure was used instead of only using an FDR correction, or only using an uncorrected threshold for the following reasons. Only using FDR correction means that actual t-thresholds vary considerably depending on the size of the search space, and makes it difficult to compare activations in whole brain and region of interest (ROI) analyses. Only using an uncorrected threshold brings the risk of excessive false positives in larger search volumes because of the multiple comparison problems. Calculating the critical t-value for both methods and using the more stringent of the two however ensures that all results are protected against excessive false positive rate while at the same time imposing a similar minimal requirement of $p<0.005$ even in small ROIs.

For the monetary reward localizer, analyses were performed in the entire brain. Most of the analyses regarding the drumming experiment were conducted in the ROI only to provide maximum power to test our hypothesis.

In order to localize reward sensitive regions of the caudate, HMR- NMR contrast images of the monetary reward task of the single participants were entered into one-sample t-tests to instantiate a random-effects group analyses. On the basis of the literature emphasizing the role of the caudate in interpersonal synchrony, reward and prosocial behavior, we aimed to specifically test the involvement of this ROI. We therefore multiplied the thresholded and binarised group t-map described above with a binary volume containing ones in the caudate and zeros elsewhere (obtained from the WFU Pick Atlas Tool, http://www.fmri.wfubmc.edu/download.htm) using the ImCalc function in SPM. Later, the resulting overlap image was used as a caudate-reward mask in order to perform small volume corrections for the results of the drumming experiment to explore the involvement of reward related caudate in our task.

For the drumming experiment, we performed the random-effects group analyses using t-tests for the contrasts *synch* - baseline, *asynch* - baseline, *synch* - *asynch* and *asynch* - *asynch*.

Two sets of multiple regressions on the second level were performed: Due to the substantial differences detected in ease of rhythm imitation across participants in the training period, we used the obtained values as covariate in order to analyze the link between participant's ease of rhythm imitation and their brain activity. Similarly, we employed a multiple regression analysis with number of pencils picked up in the prosocial test, in order to explore the brain regions showing correlation between synchronous or asynchronous drumming in the first two runs of the drumming experiment, and the number of pencils participants collected to help the in-synch or out-of-synch experimenter of the manipulation run, respectively, after scanning.

4.3. Results

Behavioral Results

1) Drumming Performance during Scanning:

Mistakes: Trials of drumming were inspected for three types of mistakes done by the participant: missing a note, stopping to play after several notes or skipping an entire trial or playing the rhythm wrongly, mainly by playing the wrong beats. A three (mistake type) x two (condition: experienced asynchronous or synchronous drumming) repeated measures ANOVA revealed neither a significant main effect of mistake type nor of drumming condition nor an interaction between the type of mistake and drumming condition on the number of trials with mistakes (see Supporting Information S3 and Table S3).

Individual Beat: Comparing the timing of each button press of the participant with the timing of the button presses that were requested by the given rhythm, indicated that all participants demonstrated negative asynchronies (i.e., their button presses were before the "requested" time) in each trial (first note is taken as start of the rhythm and has a 0 ms asynchrony and is not taken into account). The mean and standard deviation of asynchronies relative to the demonstrated rhythm can be found

in the Supporting Information Table S4. By averaging the mean accuracies over all 9 note per trial we found no significant differences ($t_{(17)} = -2.0$, $p = 0.059$) between the *synch* condition (mean ± SD: -48.6 ±16.9 ms) and in the *asynch* condition (mean ± SD: -43.7 ± 15.2 ms). Analyzing the variability of the beats of the participants we also averaged the standard deviations of each participant drums over all 9 notes per trial. Participants were more variable ($t_{(17)} = -5.5$, $p < 0.001$) in drumming in the *asynch* condition (mean of SD ± its SD: 45.2 ± 9.0 ms) than in *synch* condition (mean of SD ± its SD: 30.2 ± 8.7 ms) . Furthermore, a 9 x 2 repeated measures ANOVA (mean asynchrony of all 9 individual notes x condition) tested if there are timing differences in the beats played by participants within the different drumming conditions (synch or asynch). There was no main effect of condition ($F_{(1,17)} = 4.1$, $p = 0.059$). Furthermore, we found a main effect of the note ($F_{(8,136)} = 230.8$, $p < 0.001$) and significant interaction between the note and condition ($F_{(8,136)} = 13.7$, $p < 0.001$, for all p values the Greenhouse-Geisser sphericity correction was applied). The same 9 x 2 repeated measures ANOVA was performed on the standard deviations (standard deviation of mean asynchronies of each individual note x condition) in order to test whether there were variability differences in the beats played by participants between the different drumming conditions. We found a main effect of condition, note and an interaction (condition: $F_{(1,17)} = 30.8$, $p < 0.001$; note: $F_{(8,136)} = 46.2$, $p < 0.001$; interaction: $F_{(8,136)} = 4.6$, $p < 0.01$, for all p values the Greenhouse-Geisser sphericity correction was applied). Please see Table S4 for the means and the standard deviation of the asynchronies of the participant's button presses relative the requested times of the rhythm.

2) *Ease of Rhythm Imitation*: Participants' ease of rhythm imitation was evaluated during training according pre-defined criterion on 5 point scale (see Supporting Information Table S1). The mean ease of rhythm imitation rating was 3.1 (SD = 0.98) on that 5 point scale with substantial differences across participants. The scores of the ease of rhythm imitation of single participants correlated with their number of mistakes during drumming during scanning ($r = -.45$, $p < 0.05$, one tailed), their perceived difficulty of the rhythm ($r = -.45$, $p < 0.05$, one tailed), and their self-judged concentration needed to play the rhythm ($r = -.52$, $p < 0.05$, one tailed). Thus, participants who acquired the rhythm easier and faster (higher numbers) made less mistakes during scanning, experienced the rhythm as being less difficult and they reported to have needed less concentration to drum than those participants who had more difficulties to learn to drum the rhythm.

3) Prosocial Commitment Test: Participants collected more pencils when the main experimenter 'accidentally' dropped 8 pencils in front of the participants when she had been a synchronous drum partner (mean = 5.22, SD = 3.42 pencils) compared with when she had been an asynchronous drum partner (mean = 1.44, SD = 2.13 pencils) in the manipulation run (see Fig. 1A). This difference in helping effort was highly significant between conditions ($t(16) = 2.8$, $p < 0.05$), demonstrating more prosocial commitment towards the experimenter if she had drummed synchronously in the manipulation run, right before dropping the pencils.

To investigate if this effect was primarily due to the role of the experimenter in the manipulation run, we analyzed the number of pencils picked up using a 2x2 ANOVA (sync or async during the first two runs of the drumming experiment x sync vs async during the (third) manipulation run). This revealed a significant main effect of role played in the manipulation run ($F_{(1, 17)} = 6.4$, $p < 0.05$), but not for the role played in the first two runs of the drumming experiment ($F < 1$), and the interaction was not significant ($F < 1$). To further investigate the role of the experimenter during the first two runs and the manipulation run, we additionally calculated several correlations (see also "Supporting Information S2, Analysis of the role of the experimenter, for more details). The post-scanning questionnaires revealed that participants had processed and attended the color of the t-shirts of the experimenters and matched the color of the t-shirts with the color of the square in the demonstration video (indicating the drum partner) before each drumming block during scanning. This was evident from participants post-scanning questionnaires (see Supporting Information S2 for details). Participants' report of how much fun it had been to play with a particular colored experimenter depended both on the role played by that experimenter during the first two scanning runs (Pearson's $r = 0.64$, $p < 0.01$) and during the third, manipulation, run (Pearson's $r = 0.51$, $p < 0.05$). The same was true for reports of how much they liked that particular colored experimenter (Pearson's $r = 0.80$ $p = 0.001$ and Pearson's $r = 0.66$ $p < 0.001$, respectively). These positive correlations further indicate that participants not only helped the synchronous experimenter more but also experienced more fun and liked drumming more with the in-synch experimenter. This provides further evidence that the reward system might be triggered by synchronous activity.

4) The Interaction between the Ease of Rhythm Imitation in the Training and the Prosocial Commitment: Because of the variability in ease of rhythm imitation across our participants, we explored if there is a relation to prosocial commitment after participants experienced more or less synchronous drumming. We found a marginally significant positive correlation between participants' ease of rhythm imitation and the number of pencils collected to help the synchronous experimenter of the manipulation run (Pearson's $r = 0.54$, $p = 0.065$, one-tailed; Fig. 1B, green). Note that half of our participants were tested with a synchronous experimenter and the other half with the one who was not in synchrony, resulting in reduced power by leaving only 9 participants in each subset. On the other hand, we did not find such a correlation between the ease of rhythm imitation and the helping behavior towards the asynchronous experimenter of the manipulation run (Pearson's $r = -0.19$, $p = 0.31$; Fig. 1B, red).

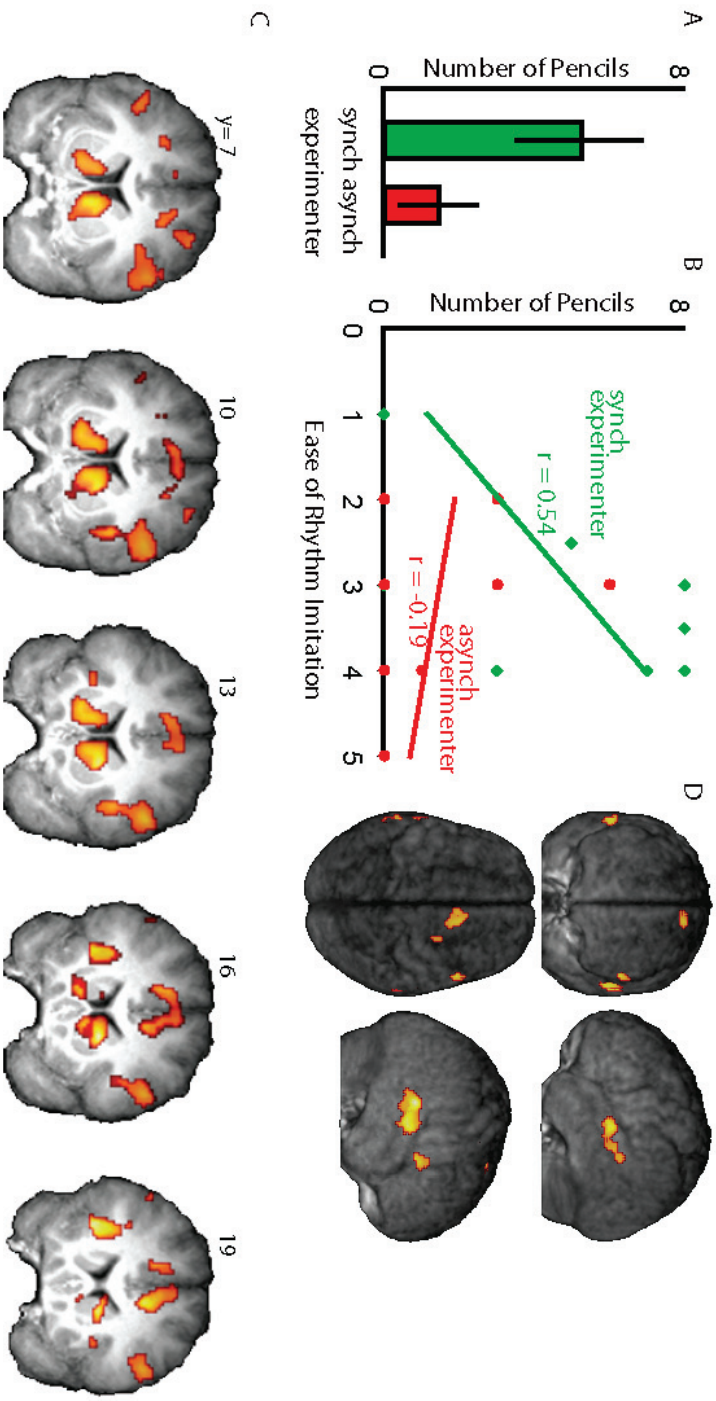
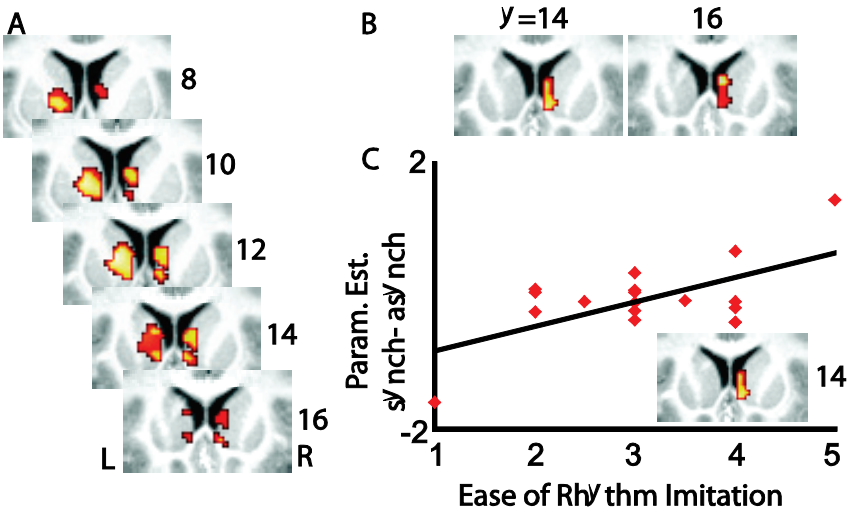


Figure 1: (A) Bar graphs showing the mean (and standard deviation) for the number of pencils picked up in order to help the main experimenter (in the prosocial commitment test) after experiencing her as synchronous drummer (green) or asynchronous drummer (red) in the last manipulation run. (B) The correlation between the number of pencils and the ease of rhythm imitation rating (green: prosocial commitment test with the main experimenter who was in-synch; red: when she was an out-of-synch experimenter). The lines represent the linear best fit and r refers to the correlation coefficient. (C) Monetary reward areas revealed from contrasting High Monetary Reward (*HMR*) with No Monetary Reward (*NMR*) blocks (*HMR* > *NMR*, $p<0.005$ uncorrected, all voxels also survive $p<0.05$ FDR correction). Clusters are superimposed on to the average T1 image derived from all participants and the coronal views are presented (D) Rendering of the average brain of all participants with contrast between asynchronous block (*asynch)* and synchronous block (*synch)* shown in red (*asynch* > *synch*, $p<0.005$ uncorrected).

Figure 2: (A) Bilateral caudate activity correlated with the ease of rhythm imitation during synchronous drumming (*synch*>baseline, p<0.005 uncorrected, all voxels also survive p<0.05 FDR correction) (B) Right caudate activity correlated with the ease of rhythm imitation for the comparison between synchronous and asynchronous drumming (*synch >asynch,* p<0.005, uncorrected; all voxels also survive p<0.05 FDR correction) (C) Illustration of the correlation identified in (B) by plotting average BOLD signal within the cluster against the ease of rhythm imitation rating. The line represents the linear best fit. Clusters in the caudate are superimposed on coronal views of the average T1 image derived from all participants.



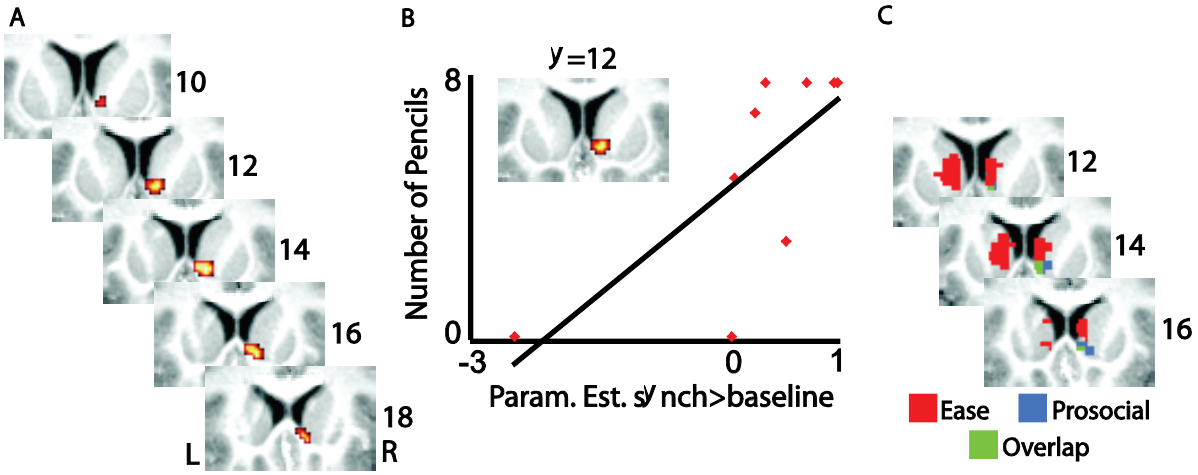


Figure 3: (A) Right caudate activity during synchronous drumming correlated with the number of pencils collected for the synchronous drummer (*synch*>baseline, p<0.005, uncorrected; all voxels also survive p<0.05 FDR correction) (B) Illustration of the correlation identified in (A) by plotting average BOLD signal within the cluster against the number of pencils. The line represents the linear best fit. (C) The overlap (green) of the correlation between brain activity during synch drumming and ease of rhythm imitation (red) and number of pencils picked up (blue) (p<0.005, uncorrected; all voxels also survive p<0.05 FDR correction). Clusters in the caudate are superimposed on the coronal views of the average T1 image derived from all participants.

Imaging Results

1) Localizer Task

We mapped the brain areas involved in monetary reward processing by contrasting the HMR (High Monetary Reward) condition with the NMR (No Monetary Reward) condition. We found significant differences in the bilateral caudate as well as in the right pallidum, right thalamus, bilateral insula, right supplementary motor area (SMA), middle cingulate, right middle frontal gyrus, right Brodann Area (BA) 6, left precentral gyrus, bilateral inferior frontal gyrus, bilateral inferior and superior parietal lobule, the left lingual gyrus, the right middle occipital gyrus and the cerebellar vermis, for monetary reward ($t(17) > 2.8$, $p < 0.005$ uncorrected, all clusters also survive $p < 0.05$ FDR correction; Fig. 1C and Table I). Our results were in accordance with the previous findings on monetary reward processing (Breiter et al., 2001; Elliott et al., 2000; Izuma et al., 2008).

2) Drumming Experiment

Synchronous and Asynchronous Drumming

Before examining our hypothesis in the ROI (see Methods), we first performed a whole brain analysis to map brain regions recruited during the various drumming conditions. We indentified the following brain areas being involved while drumming with a co-drummer who was in synchrony with the participant (*synch*> baseline: $t > 2.8$, $p < 0.005$ uncorrected; all clusters also survive $p < 0.05$ FDR correction): the right auditory cortex, the left middle temporal gyrus, bilateral postcentral gyrus, right inferior parietal lobule, right BA 44, right SMA, the bilateral pallidum (including right caudate), bilateral thalamus, left putamen and cerebellar vermis (see Table II).

The areas that were active during drumming with a co-drummer who was not in synchrony with the participant (*asynch*> baseline: $t > 2.8$, $p < 0.005$ uncorrected; all clusters also survive $p<0.05$ FDR correction) were the right auditory cortex, left middle and superior temporal gyrus, right post central gyrus, bilateral inferior parietal lobule, left superior parietal lobe, right BA 44, right pallidum, right putamen, left thalamus, and cerebellar vermis (Table III).

Using correction for multiple comparisons (FDR, $p < 0.05$) within the entire brain, as above, neither the contrast *synch>asynch* nor *asynch>synch* revealed significant differences. The results at $p < 0.005$ uncorrected ($t > 2.8$) still revealed no significant differences for *synch>asynch* but did reveal significant results for *asynch>synch* in the bilateral auditory cortices, middle cingulate cortex and preSMA (Fig. 1D).

Ease of Rhythm Imitation during Training and Synchronous Drumming

Due to the substantial differences detected across participants in the rhythm imitation during the training that could influence the experience of synchrony during scanning, we assessed whether individual differences in the training covaried with the brain activity in our ROI for reward, the caudate, during synchronous drumming. Figure 2A shows that those participants who had more ease at reproducing/imitating the rhythm before scanning activated the bilateral caudate more during synchronous drumming (second level regression analysis between brain activity during *synch* and

ease of imitation; t(17)>2.9, p <0.005 uncorrected and p<0.05 FDR corrected within the ROI, Table IV). Furthermore, the ease of rhythm imitation covaried with the activity in the right caudate for the synchronous drumming more than the asynchronous drumming (second level regression analysis between the contrast *synch-asynch* and ease of rhythm imitation; t(17)>2.9, p <0.005 uncorrected and p<0.05 FDR corrected within the ROI, Table V and Fig. 2B. To illustrate this relation more extensively, we have extracted the parameter estimates of that activation cluster for each of the 18 participants and have plotted this together with the scores for ease of rhythm imitation (Fig. 2C).

In order to test whether the reversed contrast would reveal results, we calculated a second level regression analysis between brain activity during a*synch-synch* and ease of rhythm imitation. We found very little such correlation in a whole brain analysis (since we had no hypotheses): only activity in the right amygdala correlated with ease (MNI coordinates of the peak: x = 38; y = -6, z = 26; T = 4.39, cluster size, 14 voxel) more during out-of-synch drumming than in-synch drumming (regression analysis between *asynch-synch* and ease of imitation, second level; t(17)>2.40, p <0.005 uncorrected).

Furthermore, in order to understand if the caudate activity correlates with ease of rhythm imitation because of its role in pulse keeping or in social reward, we also calculated a regression using participants' drumming behavior with circular statistics using Rayleigh test. Circular statistics is a common procedure in the tapping literature for calculating the degree of synchronization of the individual's responses to an external rhythm in order to detect the variance of asynchronies from different trials (Fisher, 1993) (the detailed explanation of the calculations can be found in (Kirschner and Tomasello, 2009). We used the mean resultant length ($\overline{R}$) of each participant from this analysis, which assesses the mean variance of asynchronies in keeping the beat, as a regressor in order to find the brain areas responsible for keeping the beat (readjusting the drumming timing to the task rhythm). BA 44 and BA 6 correlated with $\overline{R}$ (mean variance of asynchronies in keeping the beat) during asynchronous versus synchronous drumming (t (17) > 2.9, p < 0.005 uncorrected and p < 0.05 FDR corrected) and the right hippocampus did during synchronous drumming versus baseline (t (17) > 2.9, p < 0.005 uncorrected and p < 0.05 FDR corrected).

3) Prosocial Commitment

As previously reported (see Behavioral Results), we found an influence of experienced synchronous drumming during the manipulation run on prosocial commitment towards the (synchronous) drum partner (see Behavioral Results, Prosocial Commitment Test). To examine the role played by the caudate in this prosocial behavior, we assessed whether the number of pencils participants collected for the synchronous or asynchronous experimenter, respectively, after scanning could be predicted by how strongly participants activated their caudate while they experienced joint drumming that was in- or out-of-synchrony drumming during scanning (manipulation run not included). Figure 3A and 3B shows that activation in the right caudate while experiencing synchronous drumming during scanning predicted the number of pencils collected after the scanning to help the synchronous experimenter of the manipulation run (multiple regression analysis between *synch-*

baseline and number of pencils, second level; $t(14) = 2.9$, $p < 0.005$, Table VI). The results survived the FDR correction ($p < 0.05$) within the ROI. No significant correlation was found between brain activity during experiencing asynchronous drumming and number of pencils picked up for the asynchronous experimenter after scanning.

Finally, we found that the activity in the right caudate which correlated with the ease of rhythm imitation before the scanning was overlapping with the activity that correlated with the prosocial commitment after the scanning (Fig. 3C). Thus, the less effort it cost for a participant to produce the rhythm, the more activation was found in the right caudate for synchronous drumming, and the activity measured in part of this caudate (overlap) predicted the number of pencils the participant collected after scanning to help the experimenter who drummed synchronously.

4.1. Discussion

The present study is the first that investigated the neural link between synchrony in joint drumming and prosocial behavior. Based on previous studies showing that interpersonal synchrony, reward and prosocial behavior all involve the caudate in the human brain, we (1) functionally localized that brain area with a reward task, (2) measured brain activity while manipulating the degree of synchronicity between a participant and an experimenter in a drumming task performed in the scanner, and (3) examined the impact of synchronous or asynchronous drumming on the participants' propensity to help the drum partner later on. Our results suggest that the participants, who mastered the rhythm more easily prior to scanning, showed increased activity in our region of interest, the bilateral caudate, when the drum partner drummed in synchrony with them. Moreover, the amount of activity in the right caudate during synchronous drumming predicted the level of prosocial commitment, measured by the number of pencils picked up by participants in a pencil dropping test after scanning. In addition, participants who drummed with a 'synchronous' drum partner in the last part of the experiment showed more prosocial commitment towards this drum partner compared to those who drummed with an 'asynchronous' drum partner. These effects were stronger in participants that acquired the rhythm more easily. In the following we will discuss our results suggesting that synchronous drumming is socially rewarding and facilitates prosocial behavior between the synchronized individuals.

First, the analysis of the behavioral data and inspection of the number of trials with mistakes during drumming showed that participants were able to drum the rhythm in both conditions (*synch* and *asynch*) although being more variable in the asynchronous condition. In the asynchronous drumming condition, sounds of the experimenter were out of time and therefore functioned as a distracter which might have caused the higher variability in drumming performance of the participants (see (Repp, 2005). All participants tapped the individual beats before the expected time, which is consistent with the negative asynchronies found in many previous tapping studies, and which is even more pronounced in non-musicians (see (Aschersleben, 2002; Dunlap, 1910; Johnson, 1898; Miyake, 1902; Repp, 2005).

Second, the analysis of ease of rhythm imitation during training prior to scanning showed that the participants differed in time and support needed to imitate or reproduce the novel rhythm. Although, after training all participants were able to drum the rhythm, those that had needed more assistance during the initial training continued to make more mistakes during scanning, suggesting a certain continuity between the ease of acquisition and the ease of drumming during scanning. Accordingly, we had hypothesized that those participants who required more assistance initially would need to remain more focused on their own drumming during scanning and hence would be less sensitive to the differences in synchrony relative to the co-drummer. The data supports this hypothesis: the ease of rhythm acquisition before scanning predicted the magnitude of the activity difference between the synch and asynch conditions in the right caudate region that was sensitive to monetary reward (as demonstrated using the localizer task). These results are also consistent with Chapin and colleagues (2010), who showed stronger activity in the basal ganglia, including the caudate, to auditory presented syncopated rhythms when attention is directed to these rhythms. Maybe, in a similar way, our participants that found drumming easy enough could devote part of their attentions to the patterns resulting from the joint drumming with the experimenter. Two alternative explanations of this effect seem less likely. First, one could assume that the entire experiment became more rewarding for participants who acquired the rhythm more easily. However, there was no relation to stronger activity in the caudate during asynchronous drumming for those participants finding the rhythm easier to acquire, which argues against that assumption. Second, one might also argue that the increased activity in the caudate in those participants who learned the rhythm more easily is due to a more precise motor program and therefore better pulse keeping. However, the lack of significant correlation between the variance of mean asynchronies (a measure of pulse keeping) and the activity in the caudate suggests that areas other than the caudate had been sensitive to time keeping during synchronous drumming in our task.

As mentioned in the introduction, these findings about stronger activity in the caudate, which we interpret as experiencing more reward for those participants who learned to drum the rhythm more easily have face validity when considering our experience of dancing, chanting or other synchronized activities: when we struggle to perform such a task, we tend to focus our attention inwards on that task and shut out the social environment. Once we become more proficient, we open up, and start to enjoy synchronizing with others. It then becomes fun to dance, chant or drum in synchrony with others. Here, we propose that the neural correlate of this phenomenon may depend on caudate activity increasing with synchrony and ease of performance. Because studying the effect of ease of acquisition was however a secondary aim of our study, we did not prescreen subjects to ensure a homogeneous distribution of participants over the range of ease. Accordingly, our results are strongly influenced by a small number of subjects with extreme ease or unease of acquisition.

Finally, the prosocial commitment test revealed that participants helped their last drum partner more if she had drummed in-synch with them in the manipulation run that preceded the behavioral test by several minutes. These results are consistent with the behavioral studies that demonstrate a link between synchronized musical activity and prosocial behavior (Anshel and Kipper, 1988; Kirschner and Tomasello,

in press; Wiltermuth and Heath, 2009). In addition, the degree of activity in the right caudate while experiencing synchronous drumming predicted the number of pencils the individual participant would pick up in order to help the synchronous experimenter of the manipulation run. This caudate activity occurred in a region that is, as demonstrated by our localizer experiment, responding to basic monetary rewards (Izuma et al., 2008; Knutson et al., 2001; Saxe and Haushofer, 2008; Zink et al., 2008) and is known to be essential for modulating prosocial behavior (Baumgartner et al., 2008; Delgado, 2008) and for reward based decision making (i.e., modulation of a future decision based on the past experience of reward; (Balleine and O'Doherty, 2010; White, 2009). In the context of our results, this suggests that synchronized activity with a co-drummer activates reward signals in the caudate during drumming (in the scanner) and this reward-history becomes associated with the synchronized co-drummer of the manipulation run. At a later point in time, when the experimenter dropped the pencils, this reward history, associated to the experimenter that had drummed in synchrony, increased the propensity of the participant to help that experimenter. This mechanism is compatible with the role the caudate plays in non-musical decision making and reinforcement learning (Balleine and O'Doherty, 2010; White, 2009); O'Doherty, 2004; Schonberg, et al. 2007; Tricomi, et al. 2004). This link between the activity in the reward regions of the brain (the caudate) and subsequent prosocial behavior could help us understand why musicians feel so bonded after a successful jam session, but a similar explanation may also apply to cases of other, non-musical, synchronized actions such as rowing together (Cohen et al.; van Baaren et al., 2004). However, for methodological reasons we used drumming in this experiment: it was easier to have people drum than row, dance, march or chant together in the scanner. Yet, future experiments might find similar activation patterns when using non-musical tasks, as well.

Although previous behavioral studies had established the effect of synchronous activity on prosocial behavior, our results suggest that this may be true only for activities a particular individual masters easily: We found a marginally significant positive correlation between participants' ease of rhythm imitation and the prosocial commitment towards the synchronous co-drummer. There was no such correlation for the co-drummer who was not in synchrony. Similarly, the ease of rhythm imitation is also positively correlated with brain activity in the right caudate, which in turn predicted the number of pencils the participants picked up. As mentioned above, these effects depend on a small number of participants at the extreme of ease distribution.

This experiment is the first to study showing how the brain links synchronized activity to prosocial behavior. Accordingly, the sizes of these effects were unknown and there was no evidence that the effect of synchrony might be restricted to participants that master the task easily. Hence, we performed the study on a number of participants, 18, that is typical for neuroimaging studies. With hind-sight of the fact that our study finds an effect of ease of rhythm acquisition, this number may have been too small: critical findings depend on a small number of participants that acquired the task easily. As a consequence, most of our results are at the edge of significance. We therefore recommend interpreting our results with care and seeing their foremost value in channeling and inspiring future research. Specifically we believe to afford the field experimental leverage on the relation between synchrony

and prosocial behavior by providing new testable hypothesizes: (a) the effect of interpersonal synchronized actions on brain activation and prosocial behavior depends on participants that master the task well enough to have free resources to attend to the level of interpersonal synchrony, and (b) the effect of synchronized behavior on prosocial behavior is conveyed by the reward sensitive caudate. Our data is compatible with both hypotheses. However, for the data to provide strong evidence for these hypotheses, the effects in the present study are too close to significance levels and too often dependent on a small number of participants at the extremes for our variables of interest. For example, the effect of ease could be better assessed in a study that would preselect a sufficient number of participants at the extremes of the ease distribution to ensure that correlations would not depend on a small number of individuals at these extremes. The effect of synchronized activity itself would be better studied in a full group of participants preselected to master the task easily. This would provide more statistical power to compare brain activation during synchronous and asynchronous drumming and test the link between brain activity and prosocial behavior. Finally, experiments that compare musical and non-musical synchronized activities would help clarifying whether our findings are limited to music.

Another question for future research might be to identify the nature of the psychological states that represent the psychological correlate of our neural findings. Given the synchrony dependent activity in monetary reward regions we measured, it would be interesting to ask whether any enjoyable task performed with someone else would increase prosocial behavior towards that person. However, Kirschner and Tomasello (2010) showed that children engaging in a musical activity involving synchrony helped their co-musicians more but children engaging in a similar, but non-musical/non-synchronous game did not (Kirschner and Tomasello, 2010). (Kirschner and Tomasello, 2010; Kirschner and Tomasello, in press)Alternatively, one might question whether synchrony might matter at all, or whether the asynchronous drumming condition might simply have been more difficult, and the resulting sense of effort discouraged future prosocial behavior and reduced caudate activity. Two arguments speak against that. First, we found not more mistakes in the asynch than the synch conditions, as one would expect if there was a large difference in difficulty. Second, although asynch drumming was more variable than synch drumming, using variability of drumming as a predictor for caudate activity did not yield significant correlations in either direction. However, future studies may want to investigate more specifically which mental states are the causal link between synchrony and prosocial behavior to increase our understanding of these effects.

In conclusion, we provide preliminary neural evidence for why humans engage regularly in episodes of synchronized group activities (e.g., chanting, drumming, dancing, and marching). Our data suggests that the caudate (which also responded to monetary reward) transforms synchronized activity with someone into the common currency of basic reward activity, and that a history of such reward activity with a particular person influences future decisions to act altruistically towards that person, thereby increasing group cohesion. Although this social bond following synchronized behavior has been well studied in behavioral studies, with this study we generate hypotheses of why synchronized activity and its effects on affiliation might be so universal by suggesting that it ties into the brain's basic reward system. Finally, we

provide preliminary evidence that these effects depend on the individual being skilled in music making. While this effect should be replicated in a sample of participants preselected to systematically cover the range of possible skill, this finding could help explain why cultures encourage people to train musical skills. Finally, we expect that similar effects exist for non-musical activities performed in synchrony. We trust that our study will spark new research that will confirm these effects in larger samples, disentangling the pathways linking synchronized activity, brain reward systems and prosocial behavior, thereby systematically exploring the modulating effect of experience and skill in this regard.

Table I. Contrast between the High Monetary Reward and No Monetary Reward (HMR>NoMR)

Size (vox)	Hem	Area	x	y	z	T
2331	R	Caudate	14	18	4	6,14
	R	Pallidum	12	4	-4	5,54
	R	Thalamus	10	-8	6	4.68
	L	Caudate	-8	10	-2	4.65
	R	C.Vermis	6	-42	-20	4.19
1048	R	hIP1	32	-52	30	4,64
	R	Ang Gyrs/SPL	32	-66	44	4,53
	R	supMGyrs	48	-40	32	4,18
	R	MOG	34	-66	32	3,88
958	L	IPL	-30	-62	38	4,49
	L	SPL	-18	-64	40	4,03
	L	Precuneus	-12	-66	38	3,59
	R	Precuneus	8	-62	48	3,53
	L	supMGyrs	-44	-44	32	3,17
845	R	Area 6	30	-4	44	5,04
	R	MFG	32	8	56	3,58
672	R	midCingulate Crtx	12	20	32	5,28
	R	SMA	4	22	46	4,13
591	R	IFG	46	10	32	3,64
507	L	preCG	-46	-4	30	5,02
337	L	Insula	-34	18	2	5,87
	L	IFG	-40	24	26	3,84
99	R	Insula	34	22	0	4,01
60	L	Lingual Gyrus	-20	-74	-8	3,88

Results of HMR> NoMR at $p<0.005$ uncorrected (all voxels also survive false discovery rate correction at $p<0.05$). Only clusters of 10 voxels or more are reported. For each cluster, its size in voxels and hemisphere are indicated first. For each of the subpeaks of the cluster, the cytoarchitectonic areas (based on the anatomy toolbox ((Eickhoff et al., 2005)) for SPM) followed by their MNI coordinates and t-value are reported. See Table S5 for abbreviations.

Table II. Contrast *synch*-baseline

Size (vox)	Hem	Area	x	y	z	T
21508	L	postCG	-52	-16	40	9,08
	R	BA 44	52	6	14	8,26
	L	MTG	-54	-38	8	8,1
	R	C.Vermis (III)	2	-36	-16	7,97
	R	SMA	4	-2	52	7,87
	R	postCGyrs/Area 4p	38	-26	52	7,86
	R	STG/ TE 1.1	50	-14	-4	7,49
	L	Area 2	-42	-32	42	7,45
	R	IPL	44	-46	48	7,44
	R	supMGyrs	54	-34	42	7,44
3101	L	Pallidum	-20	-4	2	6,24
	R	Pallidum	20	-6	-4	5,55
	R	Caudate	14	6	8	4.65
	R	Thalamus	12	-12	4	5,29
	L	Thalamus	-12	-14	4	5,28
	L	Putamen	-18	4	8	4,81

Results of synch-baseline at $p<0.005$ uncorrected (all voxels also survive false discovery rate correction at $p<0.05$). Only clusters of 10 voxels or more are reported. For each cluster, its size in voxels and hemisphere are indicated first. For each of the subpeaks of the cluster, the cytoarchitectonic areas (based on the anatomy toolbox ((Eickhoff et al., 2005)) for SPM) followed by their MNI coordinates and t-value are reported. See Table S5 for abbreviations.

Table III. Contrast asynch-baseline

Size (vox)	Hem	Area	x	y	z	T
16489	L	MTG	-52	-38	8	9,38
	R	STG/ TE 1.0	52	-10	-6	9,23
	R	BA 44	52	6	14	8,61
	R	suprMarg Gyrs	52	-36	44	8,38
	R	Area 3b	44	-18	46	7,94
	L	IPL	-40	-30	40	7,62
	R	postCGyrs/Area 4p	38	-26	52	7,36
	L	STG	-62	-22	12	7,31
	R	C.Vermis (I/II)	2	-36	-16	7,97
	L	Thalamus	-14	-14	-2	7,33
	R	Putamen	24	16	0	6
	R	Pallidum	22	4	2	5,98
36	L	SPL	-30	-60	42	3,82

Results of *asynch*-baseline at $p<0.005$ uncorrected (all voxels also survive false discovery rate correction at $p<0.05$). Only clusters of 10 voxels or more are reported. For each cluster, its size in voxels and hemisphere are indicated first. For each of the subpeaks of the cluster, the cytoarchitectonic areas (based on the anatomy toolbox ((Eickhoff et al., 2005)) for SPM) followed by their MNI coordinates and t-value are reported. See Table S5 for abbreviations.

Table IV. Caudate correlating with the ease of rhythm imitation for the *synch* – baseline contrast

Size (vox)	Hem	Area	x	y	z	T
56	L	Caudate	-6	10	-2	3.7
14	R	Caudate	10	10	6	3.29

Correlation of brain activity in the caudate (ROI) with the ease of rhythm imitation for the *synch*>baseline contrast at $p<0.005$ uncorrected (all voxels also survive false discovery rate correction at $p<0.05$). Only clusters of 10 voxels or more are reported. For each cluster, its size in voxels and hemisphere are indicated first. For each peaks of the cluster, the MNI coordinates and t-value are reported. See Table S5 for abbreviations.

Table V. Caudate correlating with the ease of rhythm imitation for the *synch* > *asynch* contrast

Size (vox)	Hem	Area	x	y	z	T
33	R	Caudate	6	14	4	3.8

Correlation of brain activity in the caudate (ROI) with the ease of rhythm imitation for the *synch* > *asynch* contrast at $p<0.005$ uncorrected (all voxels also survive false discovery rate correction at $p<0.05$). Only clusters of 10 voxels or more are reported. For each cluster, its size in voxels and hemisphere are indicated first. For each peaks of the cluster, the MNI coordinates and t-value are reported. See Table S5 for abbreviations.

Table VI. Caudate correlating with the number of pencils (prosocial commitment) for the *synch*–baseline contrast

Size (vox)	Hem	Area	x	y	z	T
29	R	Caudate	10	12	6	3.5

Correlation of brain activity in the caudate (ROI) with the ease of rhythm imitation for the *synch*> baseline contrast at $p<0.005$ uncorrected (all voxels also survive false discovery rate correction at $p<0.05$). Only clusters of 10 voxels or more are reported. For each cluster, its size in voxels and hemisphere are indicated first. For each peaks of the cluster, the cytoarchitectonic areas (based on the anatomy toolbox ((Eickhoff et al., 2005)) for SPM) followed by their MNI coordinates and t-value are reported. See Table S5 for abbreviations.

Supplementary Information

S1) Evaluation of ease of learning abilities during training

Table S1. Description of the typical behaviors of the participants during training with respect to their 'ease of learning' ratings

Ease	Description
1	She watched the demonstration video 3 times. She could not reproduce the rhythm and asked the experimenter to show how to play the rhythm.
2	She watched the demonstration video 3 times. She was able to play the first 5 notes and missed the rest. She needed time until she was able to reproduce the rhythm correct.
3	She watched the demonstration video 2 times. Then she started reproduce the rhythm with some mistakes.
4	She was able to reproduce the rhythm after watching the demonstration video without mistakes.
5	She was immediately able to reproduce the rhythm after watching the demonstration video once.

S2) Analysis of the role of the experimenter

Given that during scanning the participants did not directly see with whom they were drumming, but only a color cue referring to the color of the t-shirt of the two experimenters, we explored if we had evidence that the participants associated this impoverished cue during scanning with a particular experimenter. We reasoned that such evidence would be present if at debriefing (see Table S2), the participant's recollection of how much fun it was to drum with the two experimenters and how much they like the two experimenters correlated with the role played (*synch* or *asynch*) by the experimenter during the beginning of the experiment (including the training) and/or the manipulation run. For each participant, we gave an arbitrary binary score of one if the participant reported to have more fun with the experimenter associated with blue and zero otherwise, yielding a binary variable with one entry per participant. A separate variable contained the same for liking (i.e., 1 if participant liked drumming with the blue experimenter more, 0 otherwise). A third and fourth variable contained one if for that participant the blue experimenter played in-synch and a zero otherwise, for the beginning of the experiment and the manipulation run, respectively. Given that synchronous activity was supposed to increase social bonding, if participants correctly associated the color cues during the experiment with the experimenters, we expected the fun and liking variable to correlate positively with the variable encoding the role of the experimenters (color of the t-shirt) both before and during the manipulation run of the experiment. Our results support our assumption. We found positive correlations between fun and the role of the experimenter before (Pearson's $r = 0.64$, $p = 0.01$) and during the manipulation run (Pearson's $r = 0.51$, $p < 0.05$). Likewise, for liking before (Pearson's $r = 0.80$ $p < 0.001$) and during the manipulation run (Pearson's $r = 0.66$ $p < 0.001$). Moreover, when we compared these correlation coefficients, we found no significant difference between

the role of the experimenter before the manipulation run and during the manipulation run for fun ($t_{(14)} = 0.417$, $p = 0.34$, one tailed) as well as for liking ($t_{(14)} = 0.545$, $p = 0.29$, one tailed).

Lastly, to ensure that the manipulation run had a contribution that was independent of the earlier part of the experiment, we used the residuals from a regression of the fun and liking scores and the role of the experimenter before the manipulation run and then correlated these residuals with the role of the experimenter during the manipulation run. This was significant for 'residual liking' (Pearson's $r = 0.71$, $p < 0.001$) and 'residual fun' (Pearson's $r = 0.7$, $p < 0.001$).

Table S2. Debriefing questionnaire

	(very hard)				(very easy)
How easy was the rhythm of the experiment?	5	4	3	2	1
How much did you need to concentrate in order to play your drums?	5	4	3	2	1
	(very much)				(very little)
How much did you like drumming with the person who was wearing a red t-shirt?	5	4	3	2	1
How much did you like drumming with the person who was wearing a blue t-shirt?	5	4	3	2	1
How much fun did you have while drumming with the person who was wearing a red t-shirt?	5	4	3	2	1
How much fun did you have while drumming with the person who was wearing a blue t-shirt?	5	4	3	2	1

S3) Mistakes

By inspecting each trial (in total 128 trials: 64 trials in each condition) per participant we identified three kinds of common mistakes (see Table S3): 1) Missing a note; 2) Stopping to play after several notes or skipping an entire trial; 3) Playing the rhythm wrongly, mainly by playing the wrong notes. A three (mistake type) x two (condition) repeated measures ANOVA showed that there was neither a main effect of mistake type ($F_{(2,34)} = 3.56$, $p = 0.07$) nor of condition ($F_{(1,17)} = 2.94$, $p = 0.11$), nor the interaction between the type of mistake and condition was significant either ($F_{(2,34)} = 2.05$, $p = 0.15$, for all p values the Greenhouse-Geisser sphericity correction was applied) on the number of trials with mistakes.

Table S3. Mean and standard deviation of the trials with mistakes for *synch* and *asynch* conditions

	Synch drumming	Asynch Drumming
Missing a note	0.44 ± 0.86	0.61 ± 0.92
Stopping to play after several notes or skipping an entire trial	0.50 ± 0.86	0.56 ± 0.78
Playing the rhythm wrongly, mainly by playing the wrong notes	1.17 ± 2.12	1.89 ± 2.19

Note: Means ± SD for the average number of trials with mistakes across participants are reported.

S4) Analysis of drumming performance

Table S4. Mean and standard deviation of the asynchronies of the participant's button presses relative the requested times of the rhythm.

MEAN	Note 2	Note 3	Note 4	Note 5	Note 6 *	Note 7	Note 8	Note 9	Note 10
synch (ms)	-68.3	-12.2	-17.1	-3.4	-291.2	-2.3	-11.5	15.3	-15.7
Asynch (ms)	-62.4	-16.4	-21.6	16.3	-315.4	-15.7	16.5	-0.25	5.9

SD									
synch (ms)	45.9	20.8	22.8	24.1	52.6	27.3	29.6	24	24.9
Asynch (ms)	67.2	30.1	34.3	47.7	77.6	33.0	33	43.8	40.3

Note: *6th beat after the break is always played too early by the participants. Asynchronies are calculated relative to the preceding note, taking into account the duration of the requested rhythm (e.g.,[(onset beat3 – onset beat 2) – (requested duration, i.e. 300ms)].

S5) Further information

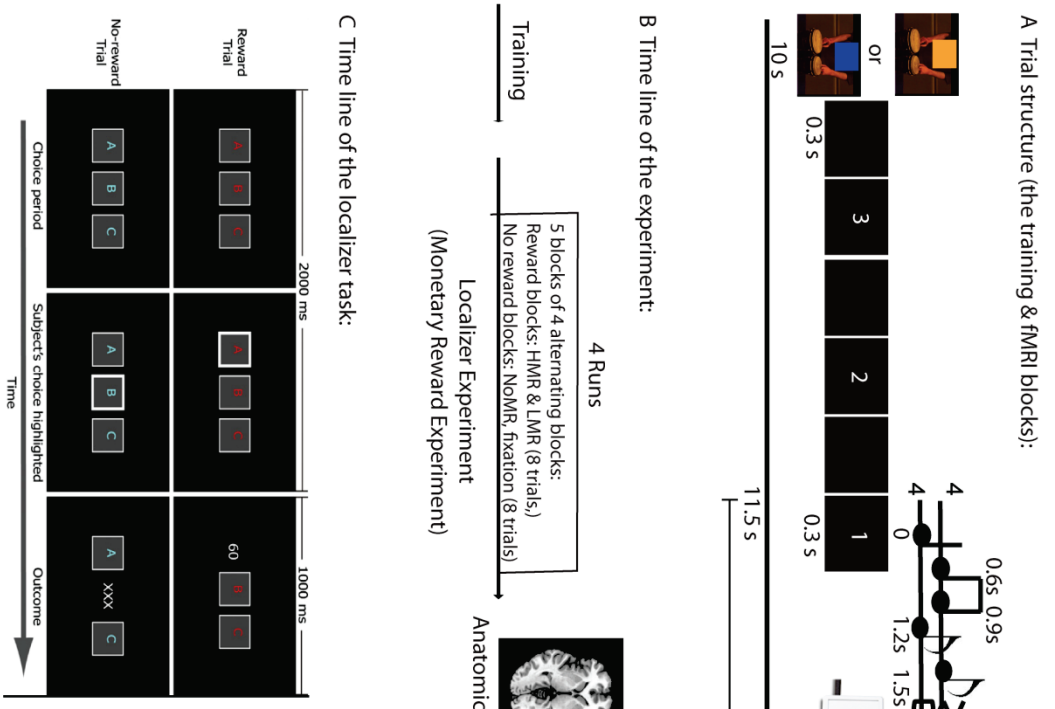
Table S5. Abbreviations used in the paper together with their meanings.

	Ang Gyrs	angular gyrus
*	BA44	Brodmann area 44
	BOLD	blood-oxygen-level dependent
	C.Vermis	cerebellar vermis
	EPI	echo-planer imaging
	fMRI	functional magnetic resonance imaging
	GLM	general linear model
	Hem	hemisphere
*	hIP1	human intraparietal area 1
	IPL	inferior parietal lobule
	MFG	middle frontal gyrus
	MOG	middle occipital gyrus
	midCingulateCrtx	middle cingulate cortex
	MTG	middle temporal lobe
	preCG	precentral gyrus
	postCG	postcentral gyrus
	SD	standard deviation
	SPL	superior parietal lobule
	supMGyrs	supramarginal gyrus
	STG	superior temporal gyrus
*	TE 1.0	primary auditory cortex
*	TE 1.1	primary auditory cortex
	Vox	voxel

All brain areas were labeled using the Anatomy Toolbox for SPM (Eickhoff et al., 2005), with areas preceded by a '*' based on probabilistic cytoarchitectonic maps.

Supplementary Materials

Figure S1: Experimental set-up and timeline and stimuli used in the fMRI experiments. (A) Trial structure of the drumming task; (B) Timeline of the whole procedure including the training, the fMRI experiment and the prosocial commitment test; (C) Trial structure of the reward localizer task.



5. Conclusion

This thesis explored how our brain processes joint actions with truly social paradigms, in which a participant directly interacted with another agent or believed to interact with one. We delineated brain areas that play a role in a series of social tasks performed during functional Magnetic Resonance Imaging (fMRI) experiments in which participants (1) engaged in joint actions with an experimenter standing next to them during a cooperation game, (2) played the same game with a computer, and (3) drummed a simple rhythm with a drum partner (Chapters 2 and 4). By employing Granger causality mapping (Chapter 3) and exploring the information flow from and to the anterior sites of the Mirror Neuron System (MNS) during our cooperation game, we gained further insight into the contribution of the MNS to joint actions. In addition to investigating the neural substrates involved when a participant acts together with an agent, we also tested how this activity relates to the actual social behavior of the drum partners (Chapter 4). This chapter briefly summarizes the results of the experiments and discusses their implications.

Moving a set dinner table often takes two people, and in doing so requires the close coordination of actions between two agents. A number of studies have proposed that the MNS is involved in responding to the actions of others by doing the same as they do (imitation) (Iacoboni et al., 1999), as well as complementing others' actions (Newman-Norlund et al., 2007b). Hence, some have argued that the MNS could promote joint actions by integrating one's own actions with those observed while individuals act together (Knoblich and Jordan, 2002; Newman-Norlund et al., 2007a; Newman-Norlund et al., 2007b; Sebanz et al., 2006; Sebanz et al., 2007). However, we argue here that during a typical joint action, unlike imitation, the task determines the nature of this integration which can vary depending on whether one is carrying out an action that is the same or opposite to that of a partner (Kokal et al., 2009). Therefore, the integration of observed actions of others with one's own actions necessary in joint actions has to be more flexible than previously thought. As opposed to previous claims, we presented evidence demonstrating that the integration is computed outside of the MNS during our cooperation game.

The first fMRI experiment of this thesis investigated the circuitry involved in task-dependent integration of observed and executed actions that distinguishes joint action from action observation and execution performed in isolation. In particular, we tested the degree to which this process occurs within or beyond the MNS (Chapter 2). To do so, we created a real-time joint action paradigm in which participants acted together with an experimenter in shaping sticks of a game box to create a geometrical shape (joint action conditions). Depending on the goal of the trial (i.e forming an angle or a straight line respectively), in some trials the participant performed a similar action to that of the experimenter and in some trials he/she performed the opposite actions. In addition, the participant (a) passively watched the experimenter moving her stick alone or (b) moved his/her stick alone. Identifying the common voxels for both (a) observation and (b) execution, revealed activity in the putative MNS (pMNS) of

our participants corresponds to those areas previously reported in the literature such as; the premotor (BA6, BA44), parietal (SI, SII, IPL) and high-level visual areas.

Given that engaging in joint actions requires the integrative processing of two streams of information (visual input and motor output) corresponding to the two agents' actions depending on the task requirements, we mapped the brain areas specifically involved in this integration by comparing the activity during joint actions to the activity during the sum of action observation and solo execution. We formulated this as follows: if integration > 0 then (joint action = observation + execution + integration) > observation + execution. A network of brain areas (integration network) showed evidence for this integration process in the prefrontal, posterior parietal and temporal lobe adjacent to the pMNS. Although both the integration network and the pMNS were in anatomically similar locations, voxels common to both networks were rare and restricted to the superior parietal lobe (SPL) and the middle occipital gyrus (MOG). Importantly, there was no overlap in the premotor cortex between regions showing evidence of integration and the pMNS. This suggests that, as opposed to previous claims, the integration of observed actions of others with one's own actions during joint actions is likely to be computed outside of the pMNS in the premotor cortex (Kokal et al., 2009).

Further investigation of the functional properties of the pMNS in joint action conditions using region of interest (ROI) analysis revealed significant activity above baseline in all ROIs of the pMNS. This suggests that although the pMNS is not involved in the integration process directly, it nevertheless plays a role in joint action. Therefore, we proposed that joint action might be a dual process: the MNS transforming the observed actions into representations of similar actions (common code) allowing one to tune his/her actions to the expected actions of the other without lagging behind due to the latencies of the visual and motor systems. The integration network, on the other hand, seems to play a role in utilizing these common codes to select the most adequate action in order to flexibly tune one's own actions to those of others.

These results are in line with the theoretical papers re-evaluating strong claims previously made about the key role of the MNS in grounding joint actions. In an influential paper, Pacherie and Dokic (2006) argue that the MNS cannot, by itself, provide a sufficient basis for our ability to engage in joint action. They claim that the function of the MNS might be to provide better control of one's own actions and the understanding of other's actions (Gallese, 2003) thus facilitating joint action control when individuals adjust their actions to those of others (Pacherie and Dokic, 2006). Likewise, Knoblich and Jordan (2002) propose that the simple perception-action matching provided by the MNS itself cannot be enough for successfully coordinating our actions with others (Knoblich and Jordan, 2002). They point out a necessity of additional machinery to modulate one's own actions in response to perceived effects of other's actions. We suggest that the integration network that we identified in Chapter 2 might be the neuronal signature of this additional machinery.

While the results of Experiment 1 revealed a network of brain areas (integration network) that are involved in the integration of a visual input and a motor output, we cannot distinguish whether this integration activity is specific for the mutual coordination that defines joint actions or whether it could be just as strong

during a task requiring only one-way coordination. Therefore, to examine whether the brain areas identified in Experiment 1 are sensitive to the mutual coordination, in Experiment 2 we scanned half of our participants a second time. Participants played the same cooperation game with an experimenter who a) adapted her actions to those of the participant (mutual coordination, true joint actions) or b) with a computer that did not (one-way coordination). By examining the activity in all ROIs of Experiment 1, we showed that brain activity in all brain areas within the integration network and the MNS were stronger while cooperating with a human agent in comparison to playing with a computer. This shows that despite the presence of similar biological movement in both conditions (given that the experimenter who was blind to the participant's actions actually played the role of the computer), these brain areas were sensitive to the presence of the mutual coordination (Kokal et al., 2009). The presence of a human finger in the display, the belief to be playing with a human agent and/or the contingency that participants detected between the human agent and their own actions (mutual coordination) must have made both networks sensitive to the presence of the social loop that characterizes joint actions (Liepelt et al., 2008). Furthermore, our results cannot be explained by the participants paying less attention to the actions of the computer, as the number of correct trials did not differ in the two conditions, nor can it be explained by differences in the time spent moving with the human agent or the computer, as the playing time did not differ significantly.

In Chapter 2, we presented evidence suggesting that the anterior sites of the MNS do not play a direct role in the integration of observed and executed actions. In Chapter 3, we focused on testing the contribution of the MNS in joint action with a different method: Granger causality mapping (GCM). We employed GCM on our fMRI data and explored the directed information flow between the anterior sites of the MNS (BA 44 and BA 6) and the brain areas previously identified in Experiment 1.

GCM of fMRI data employs a differential Granger approach (Roebroeck et al., 2005). Simulations have shown that GCM applied to fMRI signals cannot accurately infer whether information is sent from one region to another per se, however it can establish whether more information is sent from one region to another than vice versa (Roebroeck et al., 2005). By following this approach, our results revealed three main findings (1) effective connectivity between the BA 44 and BA 6 and the integrative areas, (2) the predominant direction of these effective connections, and (3) the contribution of the cerebellum in joint actions.

First, when analyses were confined to the joint action blocks, we found significantly more Granger causality (GC) from voxels within the left BA 44 (part of the MNS) to voxels within the right MOG, left thalamus, left cerebellar vermis and right cerebellum (within the integration network) than vice versa. Similarly, the GC was significantly larger from voxels within the left BA 6 (part of the MNS) to the voxels of the left cerebellar vermis (within the integration network) than vice versa (Kokal and Keysers, 2010). This implies that these two functionally separate networks are effectively connected in the service of joint actions. In addition, a direct comparison calculated between the Granger Causality maps (GCMs) relating to the joint action versus the execution blocks revealed significant differences in the GCMs originating from the left BA44 voxels to voxels within the bilateral cerebellum (these values were significantly larger during joint action blocks compared to execution

blocks). This demonstrates that the directed influence of the left BA44 on bilateral cerebellum was significantly stronger during joint actions than during execution. This implies that the information transfer between the left BA 44 and bilateral cerebellum is specific for cases in which participants need to coordinate their own actions to those of the experimenter rather than acting alone. Similar direct comparison of GCMs between joint action and observation blocks did not reveal any significant difference.

In the context of our results from Chapter 3, when an individual needs to coordinate his/her actions with the sight of another individual's actions (e.g. while creating a straight line on our game box), this task would be computationally more demanding if the participants' own actions were represented in a different code to those of the observed agent, and less demanding if they were represented in the same code. The MNS seems to facilitate the role of the integrative brain areas by representing the participant's and the experimenter's actions in the same code (Etzel et al., 2008). According to our results, the anterior sites the MNS (left BA 44 and BA 6) play an indirect role in the integration process by feeding information into the areas that are part of the integration network. This suggests that the MNS and the integration network work in concert during joint actions.

Furthermore, recent reviews (Caspers et al., 2010; Keysers et al., 2010) provide strong evidence for the fact that BA2 is systematically activated while we perform and observe the actions of others. We found that the left BA 44 evidenced significant positive dGC values with bilateral BA 2 (localized within SI of the MNS) during joint action conditions but not solo conditions (observation and execution). Thus, this suggests that the left BA 44 not only sends information to the integration network but also to the posterior sites of the MNS during joint actions. This information flow between the BA44 and the BA2 suggests that the motor and somatosensory representations interact during joint actions.

Another main finding of Chapter 3 was the predominant direction of the effective connections during joint actions. Our results revealed predominantly backwards information flow (i.e. from frontal left BA44 to more posterior areas: bilateral BA2, right MOG etc). This suggests that the premotor areas send more predictions to the sensory areas than the other way around when one engages in joint actions with another agent. This is compatible with the increasingly prominent concept of forward models (Gazzola and Keysers, 2009; Keysers and Perrett, 2004; Kilner et al., 2007; Kilner et al., 2004; Miall, 2003; Wolpert et al., 2003; Wolpert and Miall, 1996). Given that it takes approximately 200–300 ms to respond to a stimulus (Adam and Van Veggel, 1991; Michie et al., 1976) and that, when acting together with another agent, our actions would lag several hundreds of milliseconds behind the perceived actions of our partner, it seems likely that, the MNS acting as a forward model plays more of a role in overcoming the sensory delays by relying on the predicted somatosensory and visual consequences of observed and executed actions of others. This finding has been recently supported by another study where premotor regions also sent more information to visual areas than the other way around during gestural communication task, a task employing skills similar to those needed for joint action (Schippers and Keysers, 2010).

Finally, in this chapter we found that both left BA44 and BA6 sent more information to the cerebellum, than they received from it (Kokal and Keysers, 2010).

The cerebellum is known to play crucial role in motor control and is thought to be part of the forward model (Blakemore et al., 2001; Blakemore and Sirigu, 2003; Dum and Strick, 2003; Kawato et al., 2003; Stein and Glickstein, 1992). During motor control, the convergence of input from the premotor cortex and sensory structures makes the cerebellum an ideal site for calculating in real time the error between intended and actual movement, and using this error to improve motor performance (Wolpert et al., 1998). The fact that the cerebellum receives more input from the premotor cortex during joint actions compared to solo motor execution suggests that the cerebellum is of greater importance during actions performed with others such as joint actions than those performed singly. These findings emphasize that the cerebellum merits more attention in understanding of the neural correlates of joint actions.

In summarizing the results of Chapter 3 we presented the first empirical evidence, to our knowledge, demonstrating predominantly backwards information flow from the anterior sites of the MNS to the posterior (sensory) areas such as the SI and MOG during joint actions. In addition, we showed that the cerebellum is effectively connected with the premotor areas of the MNS when adjusting our actions to others'.

After gaining insight into the neural signature of a simple type of joint action (i.e. moving an arm of a clock-like device together with another agent), we extended our research to a different type of joint action, namely music making. In Chapter 4, we described an fMRI experiment together with a prosocial commitment test that investigated the neural mechanisms underlying interpersonal synchrony and its subsequent affiliated effects among synchronized individuals, respectively. Our aim was to test the prediction that the caudate plays a major role in linking the experience of being in synchrony to that of the brain's reward system, modulating the future prosocial behavior. The striatum, in particular the caudate, has long been implicated in processing both social and monetary reward (Delgado et al., 2004; Izuma et al., 2008; Saxe and Haushofer, 2008), modulating prosocial behavior (Delgado, 2008; Kosfeld et al., 2005) and voluntary motor control especially during tapping with an external stimuli (Grahn and Brett, 2007). Thus, separate studies place the caudate at the intersection between two phenomena relevant to the question at hand: 1) the capacity to synchronize with others, and 2) modulations of prosocial behavior via the reward system. However, prior to the study presented in Chapter 4 it had not been addressed whether the reward system, in particular the caudate, modulates prosocial behavior following synchronized activity.

We measured neural activity in the caudate, which we showed to respond to monetary reward in the same participants, while manipulating the degree of synchronicity between drum partners in a social drumming task. During this task, participants believed to drum with one of two co-drumming experimenters in alternating blocks in the MR scanner. One co-drummer was in-synchrony and the other out-of-synchrony relative to the participants during scanning. Our last run of the fMRI experiment was designed as a manipulation run in which only one experimenter drummed continuously with half of the participants in- and with the other half out-of-synchrony. After scanning, the same experimenter 'accidentally' dropped eight pencils in the proximity of the participant and the participant had a choice to behave

altruistically or not. We used the number of pencils collected by the participant as a measure of prosocial commitment.

The prosocial commitment test results revealed that the participants collected more pencils to help the drum partner when she drummed synchronously compared to when she drummed asynchronously with the participants before the test, during scanning. Our fMRI results revealed that synchronized drumming does trigger activity in a reward area, the caudate. In addition, the activity in the caudate during synchronized drumming in the scanner predicted the number of pencils the participant later collected to help her drum partner (Kokal, under review). These results imply that our brain transforms synchronized activity into basic reward activity, and this then, through the caudate, influences future decisions to act altruistically towards the person with whom the synchronized activity is performed. This reveals that the caudate might be the mediating structure that links the synchronized actions performed with others and the prosocial effects of engaging in joint musical activities. This provides a hint for why synchronized activity and its affiliated effects are wide-ranging in many cultures by showing that it ties into the basic reward system, just as money does.

In Chapter 4, we used music making in a social context because this activity is more amenable to the scanner environment than other cases of synchronized actions (marching, rowing etc). Our results might not be specific to synchrony in music but may apply to any forms of temporally coordinated (synchronized) actions in general. We expect that similar effects might exist for non-musical activities such as rowing in synchrony (Cohen et al., 2010), or making similar bodily movements (van Baaren et al., 2004). This possibility should be tested in future experiments using non-musical tasks.

Last, in Chapter 4 we investigated not only the behaviour outcome of synchronized actions but also the neural mechanisms that link the joint musical activity with the prosocial behaviour. Hence, our study is a pioneer in bridging different but related research questions and methods in one study. Although we recruited a sufficient number of participants for a conventional fMRI study (18 participants), discovering that the results were dependent on individual differences in rhythm imitation introduced the challenge of applying correlational analyses to only half of our participants leading to a moderate effect size. Albeit this fact, we reported the trends and marginally significant results in addition to the significant ones to inspire future studies with new hypotheses to test.

Outlook

"Individuals possess a remarkable ability to coordinate their actions with others to reach common goals" (Sebanz et al., 2006). With the accumulation of knowledge in the last decade, we are just beginning to understand the underlying mechanisms of this remarkable ability. Nonetheless, we have to underline that further research extending our knowledge about the functional properties of the brain areas reported in this thesis is crucial. We hope that the empirical evidence that we presented in this thesis will contribute to the understanding of the neural basis of medical conditions characterized by deficits in social interactions.

Over the last years, interest in the behavioural study of social music-making and the neural basis of social reward has surged as separate disciplines. In Chapter 4, we combined neuroimaging methods with an actual behavioral test in which we could investigate both neural underpinning of musical joint actions and prosocial behaviour in one study. Hence, we bridged a gap between fractured literatures in the life sciences: the study of musical behaviour and the emerging understanding of the neural basis of social reward and affiliation. We hope other researchers will follow our approach and shed more light on the understanding of the neural basis of prosociality in relation to joint activity. Although we believe in the generality of our results of this study, further research empirically testing joint actions that are not musical is crucial.

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Nederlandse Samenvatting

Om een gedekte eettafel te verplaatsen zonder dat er iets omvalt, zijn er twee mensen nodig die hun handelingen nauwgezet kunnen coördineren. Dit proefschrift beschrijft wat er zich afspeelt in de hersenen terwijl mensen samen een handeling uitvoeren. We hebben dit onderzocht door gebruik te maken van sociale paradigma's waarin de deelnemer van het experiment direct contact had met een ander persoon. Door middel van functionele Magnetische Resonantie (fMRI) hebben we hersengebieden geïdentificeerd die een rol spelen bij verschillende sociale taken. De deelnemers lagen in de MR-scanner en (1) speelden een coöperatief spel waarbij ze een gezamenlijke handeling moesten uitvoeren met de proefleider, (2) speelden hetzelfde spel als bij 1, maar nu met de computer, (3) drumden een simpel ritme met een drumpartner (respectievelijk Hoofdstuk 2 en 4). Door gebruik te maken van de analysemethode Granger Causaliteit (Hoofdstuk 3) konden we ook de informatiestroom onderzoeken van en naar de anterieure gebieden van het spiegelsysteem tijdens het spelen van het coöperatieve spel. Hiermee hebben we een dieper inzicht gekregen in de bijdrage van het spiegelsysteem aan gezamenlijke handelingen. Als laatste hebben we getest of hersenactiviteit in het beloningssysteem gerelateerd is aan het werkelijke sociale gedrag van de drumpartners (Hoofdstuk 4).

Hoofdstuk 2

Het eerst beschreven fMRI experiment in dit proefschrift onderzoekt het hersennetwerk dat betrokken is bij het integreren van geobserveerde en uitgevoerde handelingen. Deze integratie onderscheidt een gezamenlijke handeling van het observeren en uitvoeren van een handeling op zich. Recent onderzoek heeft uitgewezen dat het spiegelsysteem in de hersenen de basis is van onze capaciteit om onze handelingen met die van anderen te kunnen afstemmen (Knoblich and Jordan, 2002; Newman-Norlund et al., 2008; Newman-Norlund et al., 2007a). Met behulp van fMRI hebben we de hersenactiviteit van proefpersonen gemeten terwijl ze een coöperatief spel speelden met de proefleider. Hun taak was om één van de twee wijzers van een klok-achtig apparaat te bewegen. Ze moesten hem of één kant op bewegen of een bepaalde vorm creëren samen met de wijzer van de proefleider. In de controle condities moest de deelnemer kijken naar de bewegingen van de wijzer van de proefleider zonder zelf iets te doen (observatie) of hij moest alleen zijn eigen wijzer bewegen zonder dat de proefleider iets deed (executie). Het spiegelsysteem is betrokken bij zowel het observeren als het uitvoeren van een handeling en omvat de linker inferieure frontale gyrus (IFG) en de linker inferieure parietale kwab (IPL). De gebieden die actiever waren gedurende het spel dan gedurende de observatie en executie condities lagen naast de gebieden van het spiegelsysteem in de IFG en de IPL. Ook vonden we activiteit in de temporale en occipitale cortex (het integratie netwerk). Onze resultaten suggereren dat bij het dynamisch koppelen van je eigen

handelingen aan die van iemand anders meer gebieden in de hersenen betrokken zijn dan alleen het klassieke spiegelsysteem.

Hoewel de resultaten van het eerste experiment een netwerk van hersengebieden laten zien die betrokken zijn bij de integratie van visuele input en motorische output, kunnen we niet zeggen of deze integratie activiteit specifiek is voor een wederzijdse afstemming die karakteristiek is voor gezamenlijke handelen, of dat het net zo sterk zou kunnen zijn gedurende een taak die slechts afstemming nodig heeft in één richting.

Om te onderzoeken of de hersengebieden uit het eerste onderzoek gevoelig zijn voor wederzijdse coördinatie hebben we de helft van de deelnemers hetzelfde spel nogmaals laten spelen (a) met een proefleider die haar bewegingen aanpast aan die van de proefpersoon of (b) met een computer die dit niet doet. De resultaten hiervan laten zien dat hersenactiviteit in alle hersengebieden binnen het integratie netwerk en het spiegelsysteem sterker was tijdens het spelen met een menselijke tegenstander dan met een computer als tegenstander. Dit laat zien dat deze hersengebieden gevoelig zijn voor wederzijdse coördinatie. De contingentie die deelnemers bemerkten tussen de menselijke tegenstander en zijn eigen bewegingen (wederzijdse coördinatie) moet beide netwerken gevoelig hebben gemaakt voor de aanwezigheid van de 'social loop' die zo karakteristiek is voor gezamenlijke handelingen (Liepelt, et al. 2008).

Hoofdstuk 3

In hoofdstuk 3 hebben we ons gericht op de bijdrage van het spiegelsysteem aan gezamenlijk handelen met een andere methode: Granger causaliteitsmapping (GCM). We hebben GCM toegepast op onze fMRI data en konden daarmee de gerichte informatiestroom vaststellen tussen de anterieure gebieden van het spiegelsysteem (BA 44 en BA 6) en de gebieden zoals geïdentificeerd in het eerste experiment. GCM op fMRI data maakt gebruik van het verschil in Granger Causaliteit (Roebroeck, et al. 2005). Simulaties hebben laten zien dat GCM toegepast op fMRI signalen niet kan laten zien of informatie op zich wordt verzonden van een gebied naar een ander gebied, het kan echter wel laten zien of er meer informatie de ene kant wordt opgestuurd ten opzichte van de andere kant (Roebroeck, et al. 2005). Door het volgen van deze methode komen we tot drie bevindingen: als eerste laten onze resultaten een voornamelijk achterwaartse informatiestroom zien (dus van linker frontaal BA 44 naar meer posterieure gebieden: bilateraal BA 2 binnen SI, rechter MOG). Dit suggereert dat de premotorische gebieden meer voorspellingen zenden naar sensorische gebieden dan andersom wanneer iemand bezig is met gezamenlijke handelingen met iemand anders.

Dit is verenigbaar met het steeds prominenter wordende idee van 'forward models' (Gazzola and Keysers 2009; Keysers and Perrett 2004; Kilner, et al. 2007; Kilner, et al. 2004; Miall 2003; Wolpert, et al. 2003; Wolpert and Miall 1996). Waarschijnlijk is het zo dat het spiegelsysteem een rol speelt doordat het de sensorische vertragingen op kan vangen doordat het kan voorspellen wat de

somatosensorische en visuele consequenties zullen zijn van geobserveerde en uitgevoerde handelingen van anderen.

Als tweede hebben we gevonden dat anterieure gebieden van het spiegelsysteem in de linker hersenhelft (BA 44 en BA 6) gedurende gezamenlijk handelingen informatie uitwisselen met het integratienetwerk. Twee functioneel gescheiden netwerken worden dus effectief gekoppeld om te komen tot gezamenlijk handelen. Dit suggereert dat, wanneer iemand zijn of haar handelingen moet coördineren met die van iemand anders, het spiegelsysteem de rol van het integratienetwerk ondersteunt door de handelingen van de deelnemer en van de proefleider in eenzelfde code te representeren (Etzel, et al. 2008).

Als laatste hebben we gevonden dat zowel de linker BA44 en de linker BA 6 meer informatie sturen naar het cerebellum dan dat ze ervan ontvangen. Tijdens het uitvoeren van bewegingen convergeert input van de premotorische cortex en de sensorische structuren in het cerebellum, wat de cerebellum tot een ideale plek maakt om in real time de afwijking tussen de bedoelde en de daadwerkelijk uitgevoerde beweging te berekenen en deze afwijking te gebruiken voor het verbeteren van de motoriek (Wolpert, et al. 1998). We speculeren dat het cerebellum gedurende gezamenlijke handelingen een soortgelijke integrerende rol speelt voor het detecteren van afwijkingen in de synchroniteit tussen iemand zijn eigen handelingen en die van een ander. Daarnaast hebben we gevonden dat het cerebellum meer input krijgt van de premotor cortex gedurende gezamenlijke handelingen dan gedurende solistische handelingen. Dit suggereert dat gedurende gezamenlijke handelingen, het cerebellum meer informatie zou kunnen ontvangen over de (voorspelde) handelingen van de ander, naast het motorische commando van de bedoelde handeling die het cerebellum van de premotor cortex ontvangt gedurende solistische uitvoering van een handeling. Dit geeft het cerebellum de informatie die het nodig heeft om de eigen handelingen goed af te stemmen met die van de ander.

Hoofdstuk 4

In Hoofdstuk 4 onderzoeken we of het beloningssysteem, voornamelijk de caudate, een modulerend effect heeft op sociaal gedrag die volgt op gesynchroniseerde activiteit. We hebben de voorspelling getest dat de caudate een grote rol speelt in de koppeling tussen de ervaring van het synchroon handelingen uitvoeren en het beloningssysteem en dat deze koppeling sociaal gedrag moduleert. De caudate is in onze deelnemers betrokken bij een geldelijke beloning. We hebben neurale activiteit in dit gebied gemeten, terwijl we de mate van synchroniteit tussen drumpartners in een sociale drumtaak manipuleren. Gedurende deze taak geloofden de deelnemers dat ze aan het drummen waren met een van de twee proefleiders in afwisselende blokken in de MR-scanner. Een van de proefleiders drumde synchroon met de deelnemer, terwijl de andere proefleider niet synchroon drumde. De laatste herhaling van het fMRI experiment was ontworpen als een manipulatie waarin één van de proefleiders synchroon drumde (bij de helft van de deelnemers) of asynchroon drumde (bij de andere helft van de deelnemers). Hierna liet de proefleider, zogenaamd per ongeluk, 8 pennen op de grond vallen in nabijheid van de deelnemer, waarbij de deelnemer de

keus had om zich altruïstisch te gedragen of niet. Deze gedragstest liet zien dat de deelnemers meer pennen opraapten om de drumpartner te helpen wanneer deze synchroon had gedrumd vergeleken met als er asynchroon was gedrumd tijdens het scannen.

Onze fMRI resultaten laten zien dat het beloningsgebied, de caudate, actief wordt tijdens gesynchroniseerd drummen. Daarnaast voorspelt de activiteit in de caudate de hoeveelheid pennen die de deelnemer later opraapt om zijn of haar drumpartner te helpen. Deze resultaten impliceren dat onze hersenen gesynchroniseerde activiteit transformeren in basale beloningsactiviteit. Dit beïnvloedt, door middel van de caudate, toekomstige beslissingen om altruïstisch gedrag te vertonen tegenover de persoon met wie gesynchroniseerd is gehandeld. Dit laat zien dat de caudate de mediërende structuur is die gesynchroniseerd gedrag met anderen koppelt met de sociale effecten van het uitvoeren van gezamenlijke muzikale activiteiten. Dit licht een tipje van de sluier op over waarom gesynchroniseerd gedrag en de bijbehorende effecten hiervan zo wijd verspreid zijn in vele verschillende culturen door te laten zien dat het aangrijpt op het basale beloningssysteem, net zoals geld dat doet.

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Dear Groningen and its unique social life: dear heroes of the bar Paard van Troja on Thursday nights, thanks for the Friday-morning-headaches, dear Astro-people and their greatest friendship and parties, dear Bulgarian gang, dear Turkish gang, dear Liga, Terence, Katrien, Mateo, Hans, Ramona, Ana, Brani, thank you all for many things we did together, those were wonderful moments!

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Dear Grotebeer straat family (Nikola, Boris, kitty), thank you all of you for our cozy home and precious daily moments. Special thanks for unforgettable relaxing moments before and after work (meow, meow, the radio is on, plays silly music, the smell of the coffee from the kitchen, sleepy soft conversations, breakfast-mreakfast on the white table; great dinners, lekker banitza, nazdrave, discussions, famous Bulgarian jokes which I don't get at all, LPs-yes, at nights we do care about music-, watching movies, documentaries or Top Gear, meow, meow). Dear Nikola, thank you for all the support, joy and care during both good and bad times since we met. Thank you for everything we shared!