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Reply to comment

# Motor control may support mirror neuron research with new hypotheses and methods
# Reply to comments on "Grasping synergies: A motor-control approach to the mirror neuron mechanism"

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We are grateful to all commentators for their insightful commentaries and observations that enrich our proposal. One of our aims was indeed to bridge the gap between fields of research that, progressing independently, are facing similar issues regarding the neural representation of motor knowledge. In this respect, we were pleased to receive feedback from eminent researchers on both the mirror neuron as well as the motor control fields. Their expertise covers animal and human neurophysiology, as well as the computational modeling of neural and behavioral processes. Given their heterogeneous cultural perspectives and research approaches, a number of important open questions were raised. For simplicity we separated these issues into four sections. In the first section we present methodological aspects regarding how synergies can be measured in paradigms investigating the human mirror system. The second section regards the fundamental definition of what exactly synergies might be. The third concerns how synergies can generate testable predictions in mirror neuron research. Finally, the fourth section deals with the ultimate question regarding the function of the mirror neuron system.

Before discussing the important observations risen by commentators (Enticott [1], Frey and Chen [2], Naish and Holmes [3], Casile [4], Pezzulo, Donnarumma, Iodice, Prevete and Dindo [5], Santello [6], Swinnen and Alaerts [7], Cattaneo [8], Candidi, Sacheli and Aglioti [9], Cavallo, Ansuini and Becchio [10], de C. Hamilton [11]) we wish to stress the almost unanimous awareness that we indeed have a problem. Human mirror neuron research has almost ended up in a theoretical *cul de sac*, and we are in need for new falsifiable models on the function of this system [12]. We are very pleased to observe that our aim to infuse some fresh blood, coming from more mature fields of research, was appreciated by almost all commentators, giving raise to intriguing new suggestions.

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## 1. Measuring synergies during action observation

First of all we agree that no strong parallel could be drawn between monkey and human research [1,2]. In fact, these research streams often use incommensurable methods. We had exactly this in mind when we focused on Transcranial Magnetic Stimulation (TMS) research, which represent the best tool to study the human mirror mechanism [3]. In fact, TMS is first of all a very effective tool to study the motor system and this matches our proposition that methods and models used in motor neuroscience could inform future research on the mirror mechanism – a proposition shared by many commentaries [4–6].

However, we agree that any novel approach needs clear definitions and clear methods to measure and/or interfere with motor synergies during action observation [1,3]. If on one hand TMS-evoked electromyographic (EMG) activities during action observation are well characterized, these might be suboptimal to investigate complex TMS-evoked hand synergies [3,7,8]. On the other hand, TMS-evoked kinematics might be a promising tool [3,8], although it was correctly suggested that particular care is given to the different electromechanical delays that could characterize different body parts ([8]; see [13] for forearm muscles and [14] for some preliminary data on the tongue). The electromechanical delay, which is the delay between the onset of muscle activation and the onset of force or motion, should be carefully investigated. In fact, early studies observed quite long delays during voluntary muscle contraction [15], which were later recognized to be critically affected by instrument driven artifacts [16]. In line with this issue, we agree that we are still missing standard methods and normative data to guide the use of TMS-evoked movements as a reliable dependent variable [8].

An additional source of noise consists in the absence of experimental and data handling standards. For instance, the lack of homogeneity on the choice of control conditions and/or baseline is one of the main issues in this field [1]. The need for a methodological consensus becomes even more acute when applying the concept of synergies. In fact, synergies have been defined in different ways and linked to coordination patterns at different levels, including the kinematic, kinetic and neural ones [5,6]. In fact, when coping with the inherent complexity of synergies definition and measurement, we may even need to use new experimental paradigms including the active movement of the observer [3,9–11].

## 2. The use and definition of synergies

Importantly, we have to concur with Casile about the fact that synergies are only one of the possible models we can import from motor control literature [4]. The reasons why we proposed the synergy idea are several. First of all, it matches a Gibsonian perspective of how graspable objects directly specify affordances in a whole-hand grasping frame of reference. Furthermore, synergies intuitively avoid any artificial separation between goal and kinematics, embracing a functional and ecological perspective on behavior [3,6,10].

However, a critical point regards the level of the CNS at which synergies emerge, which may not match that of the mirror system. Indeed, as correctly stated by Cattaneo, synergies are not necessarily cortical in origin [8], rather they are classically considered as being expressed at the spinal level [17]. Nevertheless, there are different sources of evidence suggesting at least an important cortical contribution. Beside the fact that cortical stimulation elicits synergistic pattern of activities [18,19], it was shown that sensorimotor brain lesion affect the expression of synergies [20] and that neurons in the primary motor cortex (M1) seem to encode the activity of a relatively small number of functionally related groups of muscles [21]. In this vein, a recent integrative proposal suggests that recurrent activity propagating between M1, muscles, and back to M1 could maintain accurate and discrete representations of muscle synergies in M1 [22]. Nevertheless, if and how synergies map into neuronal "domains" is still an outstanding question [5,6].

In this respect, we need to be careful as the whole issue of synergy localization could be an ill-posed problem by itself. Indeed, synergies are derived from behavior and consist in a statistical description of movement, which do not necessarily have to match a localized neural representation [6]. This latter point also relates to another interesting comment. In fact, synergies offer an efficient description of voluntary movements but they do not necessarily explain the same motor variance generated by mirror neurons [8], which are fast and automatic [13]. However, we have to report that grasp synergies in the kinematic domain are usually considered to emerge from the interaction between biomechanical and neural constraints [6], which affect voluntary and involuntary movements in a similar manner [18,23].