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Self through the mirror (neurons) and default mode network: what neuroscientists found and what can still be found there

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A search for the word *self* in the Stanford Encyclopedia of Philosophy finds 1187 entries: trying to give a complete definition of this concept is not so easy. It is a great puzzle that states who we are in the world, as Alice in Wonderland once argued, afraid she could not explain herself when she came across the Caterpillar. Unfortunately, we cannot use such an excuse. Furthermore, as neuroscientists, trying to depict the self from a scientific perspective seems to get harder and harder the deeper we get into our knowledge of the brain's structure and functions. Generally speaking, the self has been seen through different lenses, according to the dominant *zeitgeist*. Classical cross-cultural studies confirmed what was intuitively conceivable: the concept of the self is highly varied across social groups and across traditions, mainly clustered around the well-characterized dichotomy between western and eastern visions (Markus and Kitayama, 1991; Baumeister and Finkel, 2010; Martínez Mateo et al., 2013), where the first is considered more independent and the latter more interconnected. In recent years, research on the self has significantly increased thanks to the cross-fertilization of disciplines that were once considered separated, such as philosophy, psychology, psychiatry, and neuroscience (Gallagher, 2011) and, to a certain extent, all the other neuro-related disciplines such as neuroethics, neuroesthetics, and neuroeconomics (Legrenzi and Umiltà, 2011). Old questions can now be addressed through recently developed – and still improving – technological tools falling under the term "neuroimaging," such as positron emission tomography (PET) or functional magnetic resonance imaging (fMRI). As the self is by definition multifaceted and polyhedral both in space and time, the flourishing of new, twisted viewpoints is thus useful to further shape and deepen our knowledge on this intriguing topic. Remarkably, the investigation on the self benefits from two of the most recent discoveries, both of them claimed to be serendipitous, made in the highly interdisciplinary field of neuroscience: the Mirror Neuron System (MNS) and the Default Mode Network (DMN).

On the one side, the MNS mechanisms first unify execution and perception of an action, with a set of neurons, ranging from premotor and supplementary motor areas to primary somatosensory and inferior parietal cortices, coding for a precise action and activated also in the observers' motor system (Cattaneo and Rizzolatti, 2009; Keysers et al., 2010). Although it has been sometimes misinterpreted (Rizzolatti and Sinigaglia, 2010), MNS is crucial for the study of the self. In fact, frontoparietal mirror neuron areas are crucial for the motor-simulation mechanisms, as well as cortical midline structures engaged in self-related information processing (Uddin et al., 2007) both in normal and pathological brain, as it can be seen for example in autistic (Enticott et al., 2012; Gallese et al., 2013) and schizophrenic subjects (Ferri et al., 2012; McCormick et al., 2012; Mehta et al., 2012).

On the other side, since 2001 it has been understood that when an individual is alerted though not actively engaged in cognitive tasks, spontaneously organized neural activity occurs in a unique constellation of brain regions called DMN and involving the posterior cingulate cortex, the precuneus, and regions of the ventromedial prefrontal cortex (Raichle et al., 2001; for an account of its discovery please refer to Raichle and Snyder, 2007; Buckner, 2012). The DMN has been consistently reported to be related to self-referential processing. In fact, activations and deactivations of DMN brain regions have often been related to self-specific processes in both healthy and diseased conditions (Gusnard et al., 2001; Sheline et al., 2009; Irish et al., 2012). Each area of the DMN seems to be involved in different subfunctions of self-referential processing (van Buuren et al., 2010), and a detailed map of the anatomo-functional DMN subregions is currently in progress (Salomon et al., 2013).

Even though some methodological caveats should be properly addressed and hopefully solved in the next years as far as resting states are concerned (Northoff et al., 2010, 2011), it is more and more evident that the boundaries between the perception of the "self" and the "other" should be pivotally found (also) around the CMS. Furthermore, being directly involved into both MNS and DMN, the self is at a crossroads between these two discoveries, and it is conceivable that in the near future such research on the self will be better valorized and further propelled through new insights that can directly derive from studying the MNS and DMN. The relationship between MNS and the self as well as its links with the study of the self and internal/external stimuli started to be discussed both for MNS (Sinigaglia and Rizzolatti, 2011) and DMN (Qin and Northoff, 2011), but a synergy between researchers from different subfields (of neuroscience and above) is strongly required to further look at the self through the mirror neurons and the DMN looking glass.

Remarkably, the first evidence of mirror neurons was obtained in monkeys with electrophysiological studies (di Pellegrino et al., 1992) and then replicated on man with neuroimaging techniques (Kilner et al., 2009; but see also Lingnau et al., 2009), electrophysiological recordings (Mukamel et al., 2010), and cerebral stimulation devices (Cattaneo et al., 2010; Avenanti

and Urgesi, 2011). Instead, the opposite happened for the DMN. Experiments were carried out first on humans, then on chimpanzees (Rilling et al., 2007), monkeys (Kojima et al., 2009; Mantini et al., 2011) and, more recently, on rats (Lu et al., 2012), thus suggesting that DMN can be a crucial aspect of the mammalian brain. Replicating the data obtained from the "Mirror Test" (Gallup, 1970, 1994; Gallup et al., 2004) and investigating the emerging self, MNS, and DMN while performing the test or during the resting state may provide deep insight, and may help describe the emergence of the self from an evolutive perspective. Moreover, DMN activity has been longitudinally elucidated across the whole life cycle, namely from its emergence in 2-day-old newborns (Gao et al., 2009) to its disappearance in dead brain patients (Boly et al., 2009). Similarly, the ontogeny of social relationship has been addressed from twin fetuses (Castiello et al., 2010) onward (Kilner and Blakemore, 2007; Lepage and Théoret, 2007). Therefore, the developmental and maturational processes and the boundaries of the self can be further addressed with a combined MNS and DMN approach. In addition, both MNS and DMN seem to be altered in neurological and psychiatric conditions (Iacoboni and Dapretto, 2006; Sandrone, 2012, 2013), and, interestingly, abnormalities and disruptions recently started to be studied as predictive behavioral markers and clinical diagnostic tools. Future investigations will be aimed at capitalizing on clinical studies on neurological and psychiatric patients in order to improve the ability of DMN in discriminating single patients from single healthy controls with increasing sensitivity and high specificity, and if possible, to realize a joint MNS and DMN-based functional taxonomy of self-related diseases. Variations in the functional connectome will then hopefully be further linked and attributed to clinical variables as well (Castellanos et al., 2013), in the framework of the widely spreading connectomic approach (Griffa et al., 2013) and of the future development of recently emerged biological technique (Chung and Deisseroth, 2013; Chung et al., 2013).

There are very good premises to add new chapters in the challenging pursuit of the boundaries of the self in the brain. A work on the self deals with the more intimate meaning of mankind and, quoting the writer Lewis Carroll, will make all of us once again "curiouser and curiouser" toward the wonderland of neuroscience.

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