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Research Report

# Revisiting mu suppression in autism spectrum disorder

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ABSTRACT

Two aspects of the EEG literature lead us to revisit mu suppression in Autism Spectrum Disorder (ASD). First and despite the fact that the mu rhythm can be functionally segregated in two discrete sub-bands, 8–10 Hz and 10–12/13 Hz, mu-suppression in ASD has been analyzed as a homogeneous phenomenon covering the 8–13 Hz frequency. Second and although alpha-like activity is usually found across the entire scalp, ASD studies of action observation have focused on the central electrodes (C3/C4). The present study was aimed at testing on the whole brain the hypothesis of a functional dissociation of mu and alpha responses to the observation of human actions in ASD according to bandwidths. Electroencephalographic (EEG) mu and alpha responses to execution and observation of hand gestures were recorded on the whole scalp in high functioning subjects with ASD and typical subjects. When two bandwidths of the alpha-mu 8–13 Hz were distinguished, a different mu response to observation appeared for subjects with ASD in the upper sub-band over the sensorimotor cortex, whilst the lower sub-band responded similarly in the two groups. Source reconstructions demonstrated that this effect was related to a joint mu-suppression deficit over the occipito-parietal regions and an increase over the frontal regions. These findings suggest peculiarities in top-down response modulation in ASD and question the claim of a global dysfunction of the MNS in autism. This research also advocates for the use of finer grained analyses at both spatial and spectral levels for future directions in neurophysiological accounts of autism.



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## 1. Introduction

Social impairments ranging from the simplest form of non-verbal interaction to sophisticated social cognition are decisive elements for the diagnosis of Autism Spectrum Disorder (American Psychiatric Association, 2013). The source of poor communication has been previously searched in psychological deficits of theory of mind (Baron-Cohen et al., 1985), imitation (Rogers and Pennington, 1991) or emotion sharing (Hobson, 1986). In the last decade, discovering which brain dysfunctions may account for such impairments has become a challenging topic for social neuroscience. The first studies used MEG (MagnetoEencephaloGraphy) to explore the activity of the MNS in Autism Spectrum Disorder (Avikainen et al., 1999; Nishitani et al., 2004). Then followed EEG and fMRI studies. A busy field of research explores the hypothesis that mirror neurons are 'broken" in persons with Autism Spectrum Disorder (ASD) Within this framework, fMRI studies started to compare the activation of the frontoparietal circuit during observation and action: should the mirror neurons be broken, action observation would then not cause the same firing effects as action execution (Gallese et al., 2012; Iacoboni and Dapretto, 2006; Rizzolatti et al., 2009; Williams et al., 2006). This would impede self-other mapping and understanding of others' action goals thus leading to imitation and interaction deficits (Gallese et al., 2012; Dapretto and Iacoboni, 2006; Oberman and Ramachandran, 2007; Williams et al., 2001).

Hamilton's (2013) meta-analysis demonstrates, however, that neuroimaging studies are far from providing clear support to this hypothesis. For instance, while several fMRI studies have reported weaker responses of the mirror neuron system (MNS) in ASD persons compared with typical controls during action observation and gestural imitation (Williams et al., 2006) or facial imitation (Dapretto et al., 2005), they are challenged by more recent studies that did not find such differences in emotional tasks (Bastiaansen et al., 2011; Grèzes et al., 2009; Schulte-Rüther et al., 2011) or imitation tasks (Dinstein et al., 2010; Marsh and Hamilton, 2011). It is worth stressing that the fMRI studies use heterogeneous methodology (see Rizzolatti and Sinigaglia, 2010, for a discussion of the methodology used) and procedures that are not supposed to tap only on MNS regions: for instance observing facial expressions would involve amygdala response while observing hand gestures would not.

EEG studies examine the same hypothesis with a focus on rolandic rhythm also called mu rhythm. Indeed mu rhythm, recorded over the sensorimotor cortex at a frequency range varying from 7–11 Hz for some authors (Willemse et al., 2010; Lachat et al., 2012) to 8–13 Hz for others (Pineda, 2005), is suppressed during both execution and observation of action. It has been suggested that mu suppression is an index of MNS recruitment and reflects downstream modulation of motor cortex by prefrontal mirror neurons (Cochin et al., 2001; Muthukumaraswamy et al., 2004; Oberman et al., 2005; Pineda, 2005). However, Arnstein and colleagues have provided a more restricted picture of the links between EEG and fMRI–BOLD signals. By recording simultaneously the two neuroimaging signals during action execution and observation, they have shown that inferior parietal, dorsal premotor and primary somatosensory cortices are directly involved in mu suppression while Brodmann (BA) 44 area is only indirectly correlated with mu modulation (Arnstein et al., 2011). In this line, a study of the effects of brain damage on action execution and observation has revealed that the magnitude of mu suppression correlated significantly with lesion extent in right parietal regions but not in the inferior frontal gyrus (IFG) (Frenkel-Toledo et al., 2014). The results of these two studies suggest that mirror neurons in BA44 are not the prime source of mu suppression; however, transcranial magnetic stimulation (TMS) studies found the IFG involved in perception-action coupling during the perception of biological and non biological actions (Newman-Norlund et al., 2010; Keuken et al., 2011). Therefore, further research is needed to clarify conflicting results in studies testing the broken mirror hypothesis with different techniques. Moreover, from seven EEG studies using Oberman design of execution and observation of hand movements, four reported an absence of mu suppression (Bernier et al., 2007; Oberman et al., 2005, 2007, 2008) though limited to gestures of unfamiliar persons), while three others found no significant differences between action execution and observation (Bernier et al., 2013 for hand movements but not facial movements (Fan et al., 2010; Raymaekers et al., 2009). Studies of children with ASD show the same inconsistencies (Martineau et al., 2008 find no mu suppression during action observation while Ruysschaert et al., 2014 find similar central mu suppression in ASD and typical children).

Such conflicting EEG and fMRI evidence of a dysfunctioning MNS in autism lead several social neuroscientists to move beyond mirror neurons in our understanding of the social brain and to explore the hypothesis of a complementary role of the Mentalizing System (or TOM system). For example, Uddin et al. (2007) have suggested that the MST would enable physical simulation of actions and action goals, while the mentalizing system (including Cortical Midline Structures and Temporo-Parietal Junction) would allow simulation of mental states or evaluative simulation. Our Psycho Physiological Interaction (PPI) analysis has revealed a significant functional coupling of the MNS with the mentalizing system during imitative interaction (Sperduti et al., 2014). As regards EEG studies, Pineda and Hecht (2009) have looked at mu suppression during two kinds of ToM tasks and found mu insensitive to incorrect social cognitive inferences; they concluded that additional mechanisms are needed to make mental attributions of intentions. A way to take into account this conclusion is to change a focus limited until now to central electrodes and to look at different functions of the alpha-mu rhythm according to distinct bandwidths.

In favor of a change in focus, it is worth considering that EEG studies have restricted their exploration of the 8–13 Hz rhythm modulation to the sensorimotor regions (i.e., mu rhythms), whereas research in neurotypical subjects has shown that observational tasks produce changes in 8–13 Hz oscillations over scalp regions other than the central regions (i.e., alpha rhythms). In particular, alpha suppression to visual stimuli may reflect cortical activation whereas alpha power increase may reflect inhibitory and top-down regulatory processes (e.g., Bazanova and Vernon, 2013; Cooper et al., 2003; Klimesch et al., 2007; Klimesch, 2012; Perry et al., 2011).

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Based on these studies and recent reviews (Bazanova and Vernon, 2013; Hamilton, 2013), we argue that a EEG whole-brain approach focusing on both alpha and mu rhythms may be relevant to explore whether MNS functioning and top-down response modulation during action observation is impaired in ASD. A whole-brain approach would allow us to move beyond MNS in our understanding of the social brain. Indeed, neuroscience research has provided strong evidence of poorer performance in attention and inhibition tasks in ASD persons underlain by a frontoparietal network dysfunction (Chan et al., 2011; Murphy et al., 2014; Vara et al., 2014).

A second change in focus would follow the recent emphasis on the distinction between discrete frequency ranges (8–10 Hz or 10–12 Hz) to account for functional dissociations within mu and alpha bands (Bazanova and Vernon, 2013; Fink et al., 2005; Frenkel-Toledo et al., 2014; Pfurtscheller et al., 2000). Bazanova and Vernon (2013) concluded their review on EEG alpha activity by indicating that the human alpha rhythm represents at least two simultaneously occurring though functionally different processes: a lower alpha (or alpha 1, 8–10 Hz) and an upper alpha bandwidth (or alpha 2, 10–12/13 Hz). On the one hand, there is evidence that action observation elicited greater mu suppression in the lower band (8–10 Hz) compared to the higher mu range (10–12 Hz) (Frenkel-Toledo et al., 2014), and that focal brain damages in areas of the human MNS (the right inferior parietal cortex) reduced the magnitude of suppression of the lower (8–10 Hz) but not the upper (10–12 Hz) mu range (Frenkel-Toledo et al., 2014). On the other hand, EEG–fMRI studies confirmed this segregation, demonstrating a correlation between BOLD signal and alpha activity (Knyazev et al., 2011; Laufs et al., 2003), especially in the upper alpha band (Laufs et al., 2006). The correlated brain regions engaged the frontoparietal network (Sadaghiani et al., 2012), associated with many cognitive processes (Molnar-Szakacs and Uddin, 2013). For instance, EEG alpha power in the upper band (10–12 Hz) was more sensitive than the lower band (8–10 Hz) in the frontal cortex to cognitive interventions (Fink et al., 2011; Klimesch, 1999) and to neurofeedback training (Zoefel et al., 2011). Interestingly, Pineda et al. (2008) reported in a seminal neurofeedback study with ASD children that training focusing on the upper mu band (C3/C4, 10–13 Hz) gave better outcome compared with the lower mu band (8–10 Hz) or large mu band (8–13 Hz). The upper alpha frequency band was also sensitive to self-monitoring during social interaction (Naeem et al., 2012; Tognoli et al., 2007), and top-down inhibitory control (Klimesch, 2012). In particular, an increase in upper alpha activity is thought to represent inhibition of non-relevant information (Bailey et al., 2014; Klimesch et al., 2007; Klimesch, 2012).

We synthesized the above-reported series of results and hypothesized that ASD response to observation may differ from that of typical individuals for the upper alpha/mu band only, as this bandwidth is related to sociocognitive processes. More precisely, we hypothesized that typical (TYP) and ASD participants would show mu suppression in the sensorimotor areas (C3/C4 scalp positions) for the lower sub-band during both execution and observation of hand movement, whereas ASD would show a lack of suppression in the upper sub-band. Adopting a full-scalp EEG analysis, we tested whether alpha/mu activity in the fronto-parietal regions would differentiate ASD from TYP participants. Indeed alpha/mu modulation in the fronto-parietal regions is seen as indexing self-monitoring and top-down inhibitory control, considered as impaired in ASD.

To explore this hypothesis, the current study aimed at disentangling the functional role of the two alpha and mu sub-bands and to investigate whether these sub-bands discriminate ASD responses from neurotypical ones for distinct scalp regions. EEG recordings were compared in ASD and neurotypical groups across rest, passive observation of action, and execution of action. A full scalp analysis of the alpha-mu activity was carried, including the large band of 8–13 Hz as the two sub-bands related to lower (8–10 Hz) and upper (11–13 Hz) alpha/mu. Cortical sources were provided for more precise interpretation of the recordings at the scalp level.

In our view the hypothesis of a functional dissociation of bandwidths may account for conflicting results concerning mu responses in ASD. Because it has been hypothesized that the activity of the presumed human MNS seems more evident in the lower mu range (Frenkel-Toledo et al., 2014), we tested whether typical (TYP) and ASD participants showed distinct mu suppression in the sensorimotor areas (C3/C4 scalp positions) for the lower sub-band during both execution and observation of hand movement. Further, by adopting a full-scalp EEG analysis, we also tested whether alpha activity in the occipital and frontoparietal regions would differentiate ASD from TYP participants since alpha modulation in these regions may index self-monitoring and top-down inhibitory control, two capacities considered as impaired in ASD.

## 2. Results

### 2.1. *Mu power suppression over central electrodes*

The analysis of the large mu band (8–13 Hz) for the central electrodes revealed that both TYP and ASD participants exhibited statistically significant mu suppression over all electrodes during action execution ($p<0.01$; see Fig. 1, panel A). By contrast, only the TYP group exhibited a statistically significant mu suppression over the C5, C3, C4, C6 ($p<0.01$) and C1, C2 ($p<0.05$) electrodes during the observation of hand gestures, (see Fig. 1, panel B). Because of age differences between the ASD and TYP groups, we verified whether mu suppression was related to age of participants. We did not find any significant correlation of mu-suppression magnitude with age in both ASD and TYP groups (all $ps > 0.05$).

### 2.2. *Spectral analysis of mu suppression*

A fine-grained spectral analysis over the central electrodes revealed no difference between ASD and TYP during Rest and Execution conditions (see Fig. 2, panels A and B). By contrast, the mu suppression in the 10–13 Hz was significantly higher for the TYP participants compared to the ASD participants during the Observation condition (see Fig. 2, panel C). We found two statistical clusters for this difference in mu suppression between ASD and TYP participants during the

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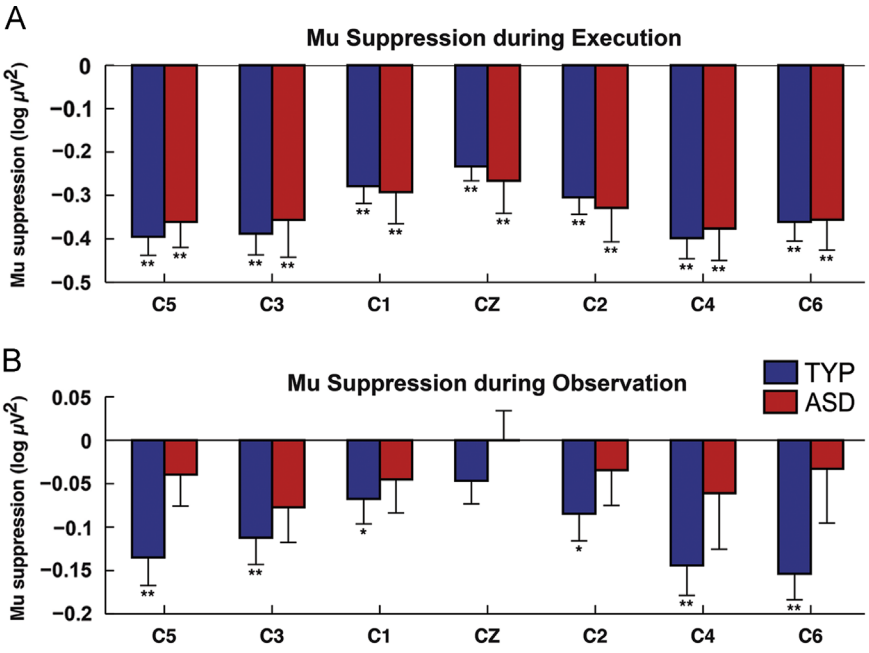


**Fig. 1 – Mu suppression values for the large-band 8–13 Hz over central electrodes (C5, C3, C1, Cz, C2, C4, C6) during Execution (A) and Observation (B) conditions. A log ratio greater than zero indicates mu enhancement; a log ratio less than zero indicates mu suppression. For the three panels, TYP participants are in blue and ASD in red. Error bars represent the standard error. Significant suppression are indicated by an asterisk, $^{*}p<0.05$, $^{**}p<0.01$. Notice that mu suppression is the log ratio of the power during the observation and execution conditions relative to the power during the resting condition.**

observation condition: one between 10.8 Hz and 11.3 Hz (CS=41.1, $p<0.05$) and the other between 11.4 Hz and 12.7 Hz (CS=105.4, $p<0.05$).

### 2.3. *Topographic analysis of scalp alpha activity during action observation*

We then extended to the whole scalp the analysis of 8–13 Hz activity (alpha rhythm) suppression during the observation condition. The analysis concerned the large alpha band (8–13 Hz), and the two alpha sub-bands (8–10 Hz and 11–13 Hz). For the large 8–13 Hz frequency band, TYP participants showed a significant suppression over the whole scalp although more strongly over the occipito-parietal region (see Fig. 3B, left; electrodes: all of them except F1, C1, CPz and Cz; CS=−243.9, $p<0.05$). The ASD participants did not show such significant alpha suppression (see Fig. 3A, left; electrodes: O1, Oz, O2, PO7, PO3, PO8, PO10; CS=−18.4, $p=0.07$).

Focusing on the lower sub-band (8–10 Hz), we found alpha suppression over the whole scalp for the TYP group (see Fig. 3B, middle; electrodes: all; CS=−251.58, $p<0.05$). The ASD group showed also a significant suppression, especially in the occipito-parietal region (see Fig. 3A, middle; electrodes: F7, F5, FC5, AF7, AF3, FT7, FC3, C5, C3, C1, CP5, CP3, CP1, P7, P5, P3, P1, PO9, PO7, PO3, O1, Oz, O2, PO10, PO8, P8, TP10; CS=−70.8, $p<0.05$).

In the upper sub-band (11–13 Hz), alpha activity of ASD participants was not significantly different during the observation condition compared to rest, whereas a significant suppression over the whole scalp was found for TYP participants (see Fig. 3B, right; electrodes: F7, F4, F6, F8, FC5, FC6, FT9, FT7, FT8, FT10, T7, T8, TP9, TP7, TP8, TP10, C6, CP5, CP2, CP4, CP6, P7, P5, P3, P1, Pz, P2, P4, P6, P8, PO9, PO7, PO3, POz, PO4, PO8, PO10, O1, Oz, O2; CS=−137.8, $p<0.05$). The between-group comparison revealed significant differences for both frontal and occipito-parietal regions, pointing to an overall greater alpha suppression over the occipito-parietal region in the TYP group and to an increase of alpha activity over the frontal region in the ASD group (see Fig. 3C, right; electrodes: F7, F5, F3, F1, Fz, F2, F4, F6, F8, AF8, FT9, FT7, FT8, FT10, T7, FC5, FC3, FC1, FC4, FC6, TP9, TP7, P7, P5, FC2, C5, C2, C4, CPz, CP2, CP4, P1, Pz, P2, P4, P6, P8, PO9, PO7, PO3, POz, PO4, PO8, PO10; CS=118.3, $p<0.05$).

### 2.4. *Source reconstruction*

Statistical analyses at the cortical level confirmed the effects observed at the scalp level during the observation condition (see Fig. 4). Significant alpha suppression was observed in the TYP group only. The suppression was located over the occipital lobe in both hemispheres (see Fig. 4B; left hemisphere: CS=−2136.4, $p<0.05$; right hemisphere: CS=−1832.9, $p<0.05$).

## 3. Discussion

Two aspects of the recent EEG literature lead us to revisit mu suppression in ASD. First and despite the fact that the mu rhythm can be functionally segregated in two discrete sub-bands, 8–10 Hz and 10–12/13 Hz (Frenkel-Toledo et al., 2014;

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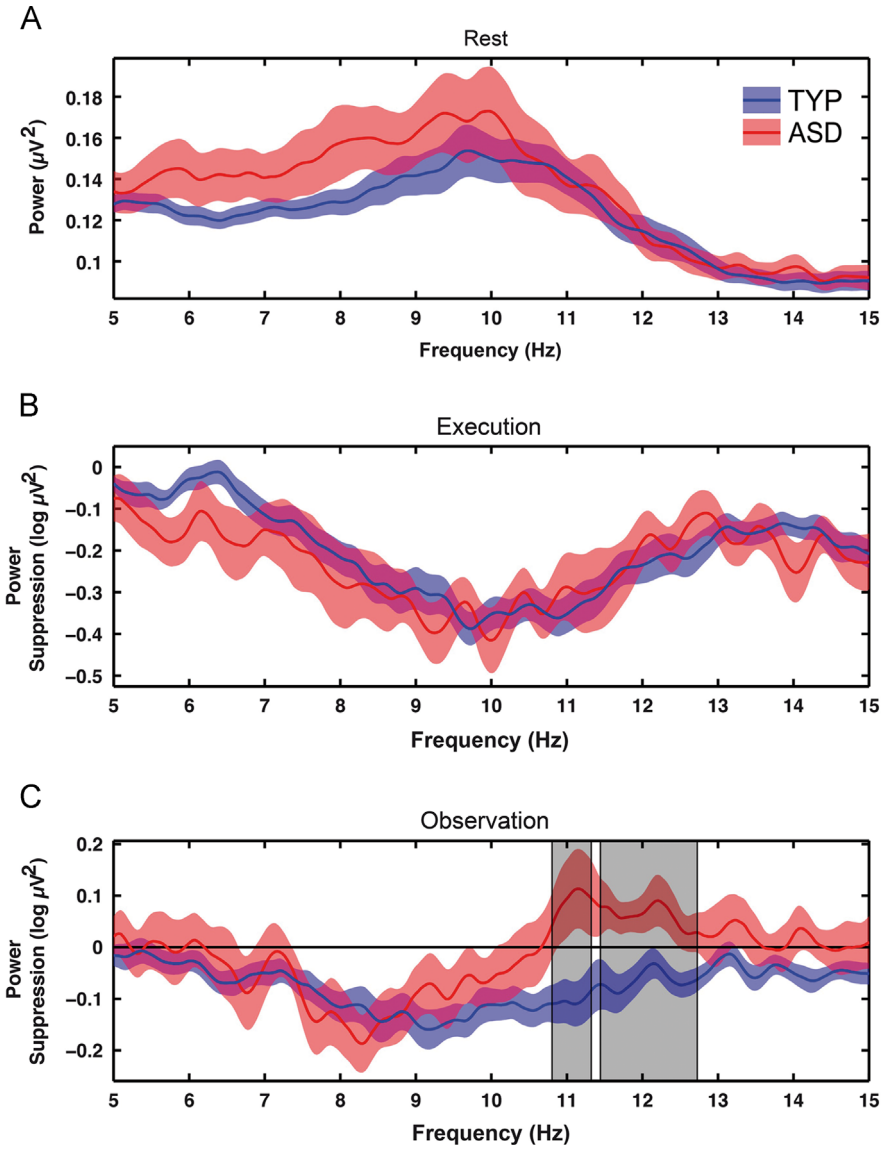


**Fig. 2 – Fine-grained spectral analysis. (A) Power spectra during the Rest. (B, C) Mu power suppression during Execution (B) and Observation (C) conditions. For the three panels TYP participants are in blue and ASD participants in red. Color shaded regions around mean represent standard error. Gray shaded regions represent significant clusters of differences between ASD and TYP participants, $^{*}p<0.05$. Notice that mu suppression is the log ratio of the power during the observation and execution conditions relative to the power during the resting condition.**

Marshall et al., 2009; Pfurtscheller and Krausz, 2000), mu-suppression in ASD has been analyzed as a homogeneous phenomenon covering the 8–13 Hz frequency. Second and although alpha-like activity is usually found across the entire scalp (Bazanova and Vernon, 2013), ASD studies of action observation have focused on the central electrodes, especially C3 and C4. The present study was aimed at testing on the whole brain the hypothesis of a functional dissociation of mu and alpha responses to the observation of human actions in ASD according to bandwidths. By combining a finer-grained spectral and whole brain analysis, our results bring a new piece of evidence that clarifies the functional significance of mu and alpha desynchronization and synchronization during action observation. In general, mu suppression has been used as an index of perception–action coupling involving the MNS (Hari, 2006; Muthukumaraswamy et al., 2004; Pineda, 2005). The lack of mu modulation during action observation in individuals with ASD has been typically interpreted as indexing a dysfunction of simulation networks such as the MNS (Bernier et al., 2007; Oberman et al., 2005; Oberman and Ramachandran, 2007), thus corroborating the 'broken mirror' theory supported by prior fMRI results (Dapretto et al.; 2005; Williams et al., 2001; Williams et al., 2006). Other EEG studies did not find such mu dysfunction (Raymaekers et al., 2009; Fan et al., 2010). Our own analyses suggest a more complex picture. When the large 8–13 Hz frequency band was concerned and the analysis was limited to C3/C4 electrodes, our results replicated an altered mu modulation during action observation in ASD participants. However, the segregation of the mu band into two sub-bands

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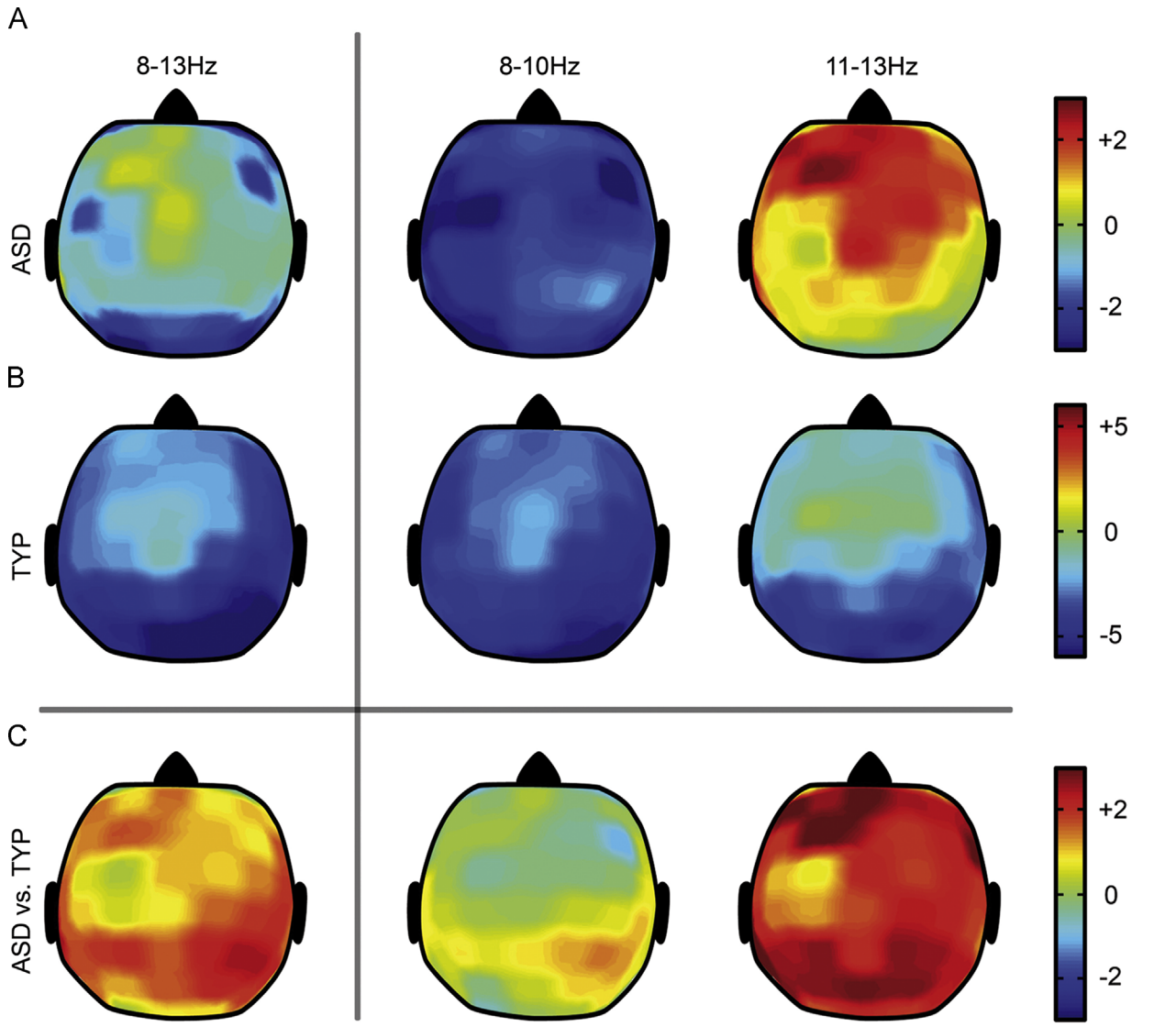


**Fig. 3 – Scalp statistical maps related to the Observation condition. Each panel shows the *t* values for large alpha band (8–13 Hz) on the left, lower alpha band (8–10 Hz) on the middle, and upper alpha band (11–13 Hz) on the right. (A, B) Alpha suppression in the ASD (A) and TYP (B) groups. Positive *t* values indicate alpha enhancement and negative *t* values indicate alpha suppression. (C) Comparison of the alpha suppression between the ASD and the TYP groups. Positive *t* values indicate reduced alpha suppression in ASD; respectively, negative *t* values indicate enhanced alpha suppression. Notice that suppression is the log ratio of the power during the observation and execution conditions relative to the power during the resting condition. Panel B has a different scales than panels A and C.**

revealed a normal response of the lower mu sub-band, in contrast with an abnormal response of the mu sub-band. Whole-brain and source level analyses showed that this altered mu modulation was related to a joint implication of an alpha suppression deficit over the occipito-parietal regions and an abnormal increase of alpha activity over the frontal regions in ASD individuals. How should this complex result be interpreted?

Studies have shown that action observation elicited greater mu suppression in the lower (8–10 Hz) compared to the higher range (10–12 Hz) in healthy subjects (Frenkel-Toledo et al., 2014), and that focal lesions in the right inferior parietal lobule (a MNS area) reduced the magnitude of mu suppression in the lower range but not the upper range (Frenkel-Toledo et al., 2014). Thus, mu suppression in the low frequency range could be a more reliable electrophysiological marker of human MNS than the whole frequency range. In this perspective our data showing similar mu suppression in the lower subband in ASD and TYP participants might reflect the fact that the MNS was functionally preserved in our ASD participants. Although further studies are required with larger samples of ASD participants, our data are consistent with findings showing no difference in mu suppression between ASD and TYP groups (Bernier et al., 2013; Fan et al., 2010; Raymaekers et al., 2009). The discrepancy between other studies might reflect symptom heterogeneity of ASD and methodological differences (e.g., familiarity and complexity of actions) (Fan et al., 2010;

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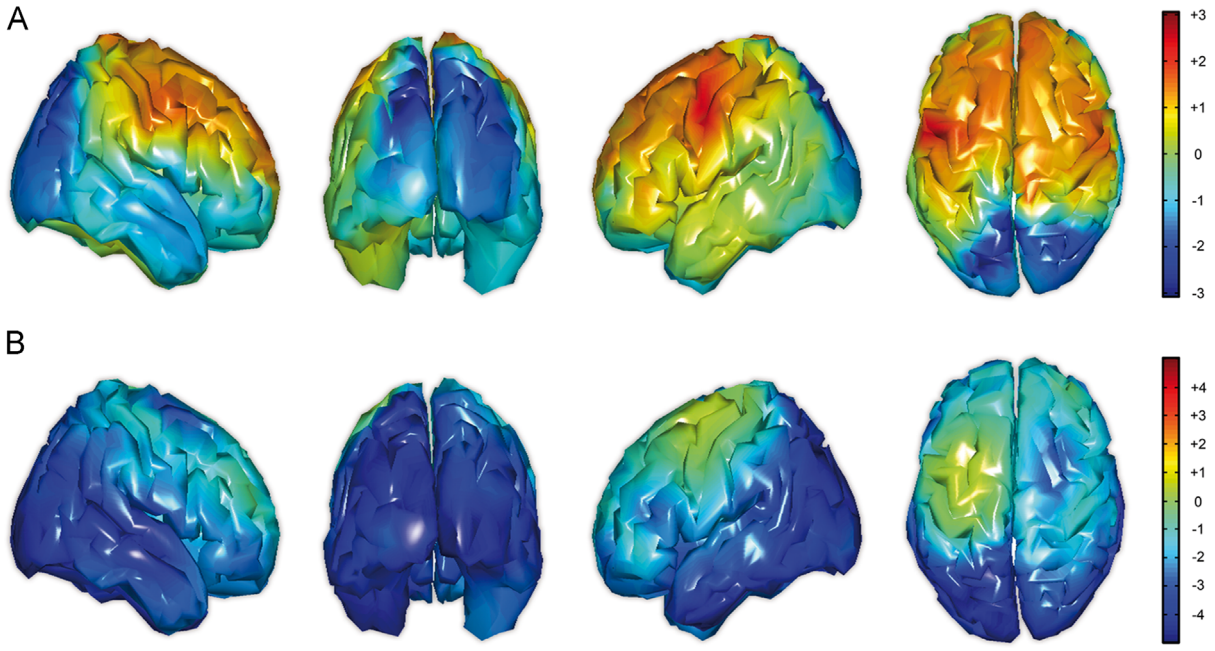


**Fig. 4 – Statistical maps of alpha suppression at the cortical level in ASD (A) and TYP (B) participants for action observation in the upper alpha band (11–13 Hz). Positive *t* values indicate alpha enhancement and negative *t* values indicate alpha suppression. Notice that suppression is the log ratio of the power during the observation and execution conditions relative to the power during the resting condition. Panel B has a different scales than panel A.**

Oberman et al., 2008) and the use of a large mu range that likely obscures important neural differences between the lower and higher parts of this range (see Frenkel-Toledo et al., 2014).

Second, an increase in the upper alpha amplitude (synchronization) has been associated with executive control (e.g., inhibitory process) and self-monitoring (Bazanova and Vernon, 2013; Jann et al., 2009; Klimesch et al., 2007; Laufs et al., 2003). According to the neural efficiency hypothesis, a greater level of upper alpha amplitude over sensorimotor regions and frontal areas in attentional tasks may reflect a top-down inhibition of task-irrelevant cortical areas or of potential interfering processes (Bazanova and Vernon, 2013; Cooper et al., 2003; Klimesch et al., 2007; Klimesch, 2012). For instance, a significant increase of 11–13 Hz oscillatory activity over sensorimotor areas was evidenced when subjects withhold the execution of a response (Hummel et al., 2002; Klimesch et al., 2007). In the same line, an fMRI study has demonstrated an enhanced frontal activation in subjects with ASD during motor inhibition and tasks requiring the inhibition of a cognitive interference (Schmitz et al., 2006). This finding suggests an increased effort to inhibit motor responses and an abnormal functioning of some brain regions involved in executive functions in ASD.

In addition to an increase of the upper alpha/mu in the frontal regions, our group of adults with ASD showed an absence of alpha suppression in the occipito-parietal regions. How should this phenomenon be explained? Human EEG studies and multiunit activity recorded in macaque monkeys have provided evidence that alpha activity decreases in occipito-parietal regions during tasks requiring attention focused on external stimuli (Bollimunta et al., 2011; Konvalinka et al., 2014; Lachat et al., 2012; Palva and Palva 2007). This alpha suppression has been interpreted as a functional correlate of cortical activation and active information processing (Klimesch et al., 2007; Rajagovindan and Ding, 2011; Romei et al., 2008). Given that action observation involves simultaneously an activation of relevant cortical regions and an active inhibition of task-irrelevant cortical regions, the lack of alpha suppression over the occipito-parietal regions and the increase of alpha activity over the frontal regions during action observation in ASD individuals might account for an inappropriate top-down response modulation. Our results among others cited above support a model in which visuomotor mapping is not just a direct matching but is subject to a top-down control and a selection of actions based on an evaluation of the current context (Hamilton, 2013; Sperduti et al., 2014; Wang and Hamilton, 2012). The fact that neurofeedback training can help normalize mu modulation in the upper mu band (Pineda et al., 2008) brings an interesting support to this top-down model at a functional level.

To conclude, we have shown that a whole brain analysis combined with a segregation of the 8–13 Hz alpha/mu band into two sub-bands reveal mixed results of normal (in the lower mu frequency band) and abnormal increase in the higher alpha frequency band during action observation in adults with ASD, in contrast with normal responses to action execution. Our findings suggest that the MNS might be functionally preserved in our sample of ASD, but that brain

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anomalies in top-down modulatory responses might be present during action observation. Further research is needed to analyze in more details how visual attention and motor inhibition are coordinated in ASD. Abnormal connectivity has been observed in ASD at the functional level (Coben et al., 2008; Khan et al. 2013; Murias et al., 2007) and at the structural level (McAlonan et al., 2005; Ecker et al., 2010; Hyde et al., 2010). For instance, Just and colleagues posit that under-connectivity between prefrontal and posterior areas may be a valid explanation of autism (Just et al., 2012), due to a lower frontal-posterior communication bandwidth, which reduces top-down influences. In line with this model, the peculiarities in ASD top-down modulation of action observation suggested by our study pave the way for further research concerning neurophysiological accounts of executive functions during attentional tasks in Autism Spectrum Disorder.

## 4. Experimental procedures

### 4.1. Participants

Ten high-functioning adults with Autism Spectrum Disorder (7 males, 3 females; M age ± SD = 33.9 ± 6.2 years; range = 21–41 years) and thirty typical adults (14 males, 16 females; M age ± SD = 28.7 ± 5.2 years; range = 20–39 years) participated in the study. All subjects had normal or corrected-to-normal vision. They were right-handed (except one individual in the ASD group). All were volunteers and had given their written informed consent according to the Declaration of Helsinki. The institutional ethical review board for Biomedical Research of the Hospital approved the experimental protocol (agreement #104-10).

The diagnosis of high functioning ASD was established by psychiatrists and neuro-psychologists with the DSM-IV-R (American Psychiatric Association, 2002), the Autism Diagnostic Interview-Revised (ADI-R; Lord et al., 1994), the Autism Diagnostic Observation Schedule-Generic (ADOS-G; Lord et al., 2000) module 4 (mean Social-communication score = 10.8, SD = 5.77), and expert clinical evaluation. None of the ASD participants had associated neuropsychiatric or neurological disorder. None was under any drug or/and intervention program or participating to another experiment during the study. They were 4 students with at least 3 years of university training, and 6 accomplished professionals with high-level specialty as graphic teacher, archivist, librarian, psychotherapist, engineer and computer programmer. None of the neurotypical participants reported a history of psychiatric or neurological disease. The control group was composed of students with at least 3 years of university training. The two groups were therefore comparable as far as academic achievement is concerned.

This paper presents the intra-individual results of a broader study using a dual EEG hyperscanning platform to acquire inter-individual data from 10 mixed dyads composed of an adult with ASD and a typical adult, and 10 dyads of typical adults.

We briefly summarize the design, which is fully described in previous papers with typical individuals (Dumas et al., 2010, 2012).

### 4.2. Dual-video acquisition

The experiment was conducted in three connected laboratory rooms, one for each participant and the third one for the computerized monitoring of the experiment. The participants were comfortably seated, their forearms resting on a small table in order to prevent arms and neck movements. They faced a 21-in. TV screen. Two synchronized digital video cameras filmed the hand gestures. A LED light controlled manually, via a switch, by an experimenter located in the recording room, signaled the session start. The output of the video records was transmitted to two TV monitors installed in the recording room allowing the experimenter to control that participants followed the requested instructions.

### 4.3. EEG acquisition

The neural activities of participants were recorded with a Brain Products (Germany) EEG recording system. It was composed of an Acticap helmet with 64 active electrodes arranged according to the international 10/20 system. The helmet was aligned to nasion, inion and left and right pre-auricular points. A 3-dimensional Polhemus digitizer was used to record the position of all electrodes and fiducial landmarks (nasion and pre-auricular points). The ground electrode was placed on the right shoulder of the subjects and the reference was fixed on the nasion. The impedances were maintained below 10 kΩ. Data acquisition was performed using two 64-channels Brainamp MR amplifiers from the Brain Products Company (Germany). Signals were analog filtered between 0.16 Hz and 250 Hz, amplified and digitalized at 500 Hz with a 16-bit vertical resolution in the range of ±3.2 mV.

### 4.4. Procedure

The experimental protocol was divided into three blocks separated by a 10 min rest. Each block comprised three runs of 2 min. A run was composed of three conditions: an observation of a prerecorded library of 20 meaningless hand gestures (observation phase, total duration: 6 min), a spontaneous imitation episode where the subjects were told that they could at will either produce hand gestures of their own or imitate the other's hand gestures (Spontaneous Imitation), and an episode where the subjects were asked to imitate a prerecorded video (Video Imitation). Each run started by a 30 s period with no view no-movement (Resting State, total duration: 4.30 min). Before each imitation condition, the subjects were asked to produce a 30 s of meaningless hand gestures (execution phase, total duration: 3 min).

At the end, a short block of calibration comprised periods of blinks, jaws contraction, and head movements of 30 s each. All conditions were presented in a fixed order for group comparison.

### 4.5. Data analyses

#### 4.5.1. EEG artifacts

Blink, muscles and head movements artifacts were filtered by optimal projection (FOP) methodology (Boudet et al., 2007).

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EEG signals were then controlled visually another time. The few remaining artifacts (<0.1% of the data, no difference between the two groups) were excluded from the analysis and we smoothed the joints by a convolution with a half-Hanning window of 400 ms in order to avoid border artifacts induced by the suppression.

#### 4.5.2. *Electroencephalography*

Instead of using selected large frequency bands, we have covered the whole spectrum (0–48Hz) with 1 Hz frequency bins, which accounts at best for the variability in frequency distributions across subjects. Following corrections, EEG data were re-referenced to a common average reference (CAR). Then a Fast Fourier Transform (FFT) was applied on 2 s sliding windows, smoothed by Hanning weighting function half-overlapping across the whole trials to control for artifacts resulting from data splicing.

Instead of restricting our analysis of the mu rhythm over C3 and C4 electrodes (Oberman et al., 2005; Pineda, 2005), we first analyzed it over a larger area of the primary sensorimotor cortex covering the left central (C5, C3, C1) and right central (C2, C4, C6) positions from the vertex point (Cz) (Kaiser et al., 2003; McFarland et al., 2000). The mu rhythm was defined as the frequency band ranging from 8 to 13 Hz topographically centered over the electrodes located at these locations. We split this large frequency band into two sub-bands: the lower and the upper alpha-mu, respectively defined between 8–10Hz and 11–13 Hz frequency ranges.

Mu suppression was calculated taking the ratio of the power during the observation and execution conditions relative to the power during the resting condition. This was done for all frequency bins separately in the case of the analyses along the spectral dimension. This ratio is used to control for variability in absolute mu power as a result of individual differences such as scalp thickness and electrode impedance. Since ratio data are inherently non-normal as a result of lower bounding, a log transform was used for analysis (Leocani et al., 1997; Pfurtscheller and Berghold, 1989). A log ratio of less than zero indicates suppression whereas a value of zero indicates no suppression and values greater than zero indicate enhancement.

Then, we conducted a spectral analysis, which consists in a fine-grained comparison of power and power-suppression across each frequency bin, without averaging over a large band.

Finally, a third analysis focused on the spatial structure of power suppression at the scalp level for the three frequency bands: 8–13 Hz, 8–10 Hz and 11–13 Hz. This analysis covered the whole scalp, thus integrating also the electrodes over the occipital, temporal, parietal and frontal regions.

#### 4.5.3. *Source reconstruction*

Source reconstruction was performed with the free open-source application Brainstorm (http://neuroimage.usc.edu/brainstorm; Tadel et al., 2011). Sensors were registered for each subject using the fiducial landmark and projection on the scalp surface of the standard Montreal Neurological Institute (MNI) template space (Colin27) (Holmes et al., 1998). The lead field was then computed using the overlapping spheres algorithm (Huang et al., 1999) with a cortical surface tessellated with 4000 vertices. We took the identity matrix for noise covariance since later analyses integrate the resting state condition. The inverse solution was calculated for each individual using Tikhonov-regularized minimum-norm estimates (Baillet et al., 2001). We calculated source activity in each frequency bin and condition, and then derived the log-ratio for mu-suppression.

#### 4.5.4. *Statistics*

To correct for multiple comparisons, significant differences were established for all contrasts using a non-parametric cluster randomization test across spatial and spectral domains (Maris and Oostenveld, 2007; Maris et al., 2007; Nichols and Holmes, 2002). This test effectively controls the false discovery rate in situations involving multiple comparisons by clustering neighboring quantities that exhibit the same effect. The neighborhood was unvaried across space (adjacent electrode over the scalp) or frequencies (side-by-side frequency bins). The permutation method provides values whose t statistics exceed a given critical value when comparing two conditions value by value. In order to correct for multiple comparisons, neighbor values exceeding the critical value were considered as a member of the same cluster. The cluster-statistic (CS) was taken as the sum of t values in a given cluster. Evaluating the CS distribution through 1000 permutations controlled the false discovery rate (Pantazis et al., 2005). Each permutation represented a randomization of the data between the two conditions and across multiple subjects. For each permutation the CSs were computed by taking the cluster with the maximum sum of t statistics. The threshold controlling the family wise error rate (FWER) was determined according to the proportion of the randomization null distribution exceeding the observed maximum CS (Monte Carlo test). Clusters containing less than three different electrodes or three different frequency bins were excluded. We used a threshold critical value of $|2\sigma|$.

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