10-2014

Biological motion processing in typical development and in the autism spectrum

Aaron Krakowski

Graduate Center, City University of New York

How does access to this work benefit you? Let us know!

Follow this and additional works at: https://academicworks.cuny.edu/gc_etds

Part of the Behavioral Neurobiology Commons, and the Clinical Psychology Commons

Recommended Citation

Krakowski, Aaron, "Biological motion processing in typical development and in the autism spectrum" (2014). CUNY Academic Works. https://academicworks.cuny.edu/gc_etds/437

This Dissertation is brought to you by CUNY Academic Works. It has been accepted for inclusion in All Dissertations, Theses, and Capstone Projects by an authorized administrator of CUNY Academic Works. For more information, please contact deposit@gc.cuny.edu.
BIOLOGICAL MOTION PROCESSING IN TYPICAL DEVELOPMENT AND THE AUTISM SPECTRUM

AARON I. KRAKOWSKI

A dissertation submitted to the Graduate Faculty in Psychology in partial fulfillment of the requirements for the degree of Doctor of Philosophy, The City University of New York

2014
This manuscript has been read and accepted for the Graduate Faculty in Psychology in satisfaction of the dissertation requirement for the degree of Doctor of Philosophy.

Date

John J. Foxe Ph.D.
Co-Chair of Examining Committee

Date

Sophie Molholm Ph.D.
Co-Chair of Examining Committee

Date

Maureen O’Connor, Ph.D.
Executive Officer

Supervisory Committee:

Jill Grose-Fifer, Ph.D.

Hilary Gomes, Ph.D.

Matthew J. Hoptman, Ph.D.

James C. McPartland, Ph.D.

THE CITY UNIVERSITY OF NEW YORK
Abstract

Biological motion processing in typical development and the autism spectrum

Aaron I. Krakowski

Advisors: John J. Foxe, Ph.D. Sophie Molholm, Ph.D.

Biological motion (BM) analysis and interpretation is a fundamental process of human neurocognition that has been only minimally explored neurophysiologically. In addition to its importance in understanding the underlying roots and development of social cognition, BM processing is a prime candidate domain for exploring the underlying etiology of social cognitive disorders such as the autism spectrum.

In an initial experiment, typical adults observed BM point-light displays of a human actor (UM) as well as their spatially scrambled counterparts (SM), in both an unattended distractor task as well as an explicit attention task. Results showed a neurophysiological response manifested as three phases of activity over parieto-occipital sites: an early (100-200 ms) automatic phase that was task-invariant; a mid-level activity (200-350 ms) that was amplified by attention; and a later phase of activation (400-500 ms) that only manifested when BM was explicitly attended.

In contrast, in follow-up experiments with typically-developing children (TDs), BM processing that distinguished UM, SM, and inverted motion (IM) occurred later (250 ms onward) and appeared as only one contiguous window of activation that was unaffected by attention. It was also observed that children with an autism spectrum disorder (cASD) demonstrated both typical BM behavioral ability as well as typical BM-related
electrophysiological activity as manifest in the interactions between group and the three BM stimulus-responses (UM, IM, SM). Notably, all three stimulus-responses individually generated similarly distinct between-group effects from quite early (129 ms) suggestive of more general visual processing dysfunctions in the disorders. In addition, a more powerful secondary analysis detected between-group effects even in the differences between the responses evoked by the UM and SM conditions, suggesting the presence of specific BM-processing dysfunctions in ASD. The role of such sensory deficits in the development of social impairments in the disorders such as in theory-of-mind is discussed.
ACKNOWLEDGEMENTS

Over the years of my career as a graduate student working toward this dissertation, there have been many colleagues and friends who, generous with their time and wisdom, have been essential to its completion. Firstly, I would like to thank my mentors, Drs. John J. Foxe, PhD and Sophie Molholm, PhD, who have both spent countless hours guiding me from the initial stages of disconnected, unpolished thoughts to manuscripts published in scientific journals. Also invaluable were my colleagues who acted as sounding boards and moral support, as well as collaborators in the research itself. These include, but are not limited to, my coauthors: Drs. Pejman Sehatpour, PhD, Simon Kelly, PhD, Lars Ross, PhD, Adam Snyder, PhD, and John Butler, PhD, and colleagues and friends: Drs. Alice Brandwein, PhD, Natalie Russo, PhD, Hans-Peter Frey, PhD, Manuel Gomez-Ramirez, PhD, Edmund Lalor, PhD, Ryan Bell, PhD, Ted Altschuler, PhD, and Gizely Andrade, as well as the other members of the three labs in which we conducted this research. I also would like to thank the lab technicians, Jennifer Montesi, Emma-Jane Forde, Sarah Ruberman, and Frantzy Acluche, who’s expertise and generosity made data-collection that much more meaningful and rewarding. I also, of course, extend appreciation to the participants and their parents without whose devotion to the scientific cause none of this research would have been possible. Lastly, but far from leastly, I would like to thank my parents and my wife whose patience and devotion over the years were a bedrock for this endeavor.
CONTENTS

Abstract ................................................................................................................................. iv
Acknowledgements ........................................................................................................... vi
Chapter I ............................................................................................................................. 1
  Point-light displays of biological motion ................................................................. 2
  Neuroanatomy of biological motion processing ....................................................... 4
  Neurophysiology .............................................................................................................. 7
  Display orientation and biological motion processing ............................................... 11
  Attention and biological motion ................................................................................... 12
  The emerging picture ...................................................................................................... 13
  The typical development of biological motion processes .......................................... 15
  Biological motion processing in the autism spectrum ............................................... 16
Chapter I: Tables and Figures ......................................................................................... 20
Chapter II ........................................................................................................................... 24
  Abstract ............................................................................................................................ 25
  Introduction ....................................................................................................................... 26
  Materials and methods ................................................................................................... 27
    Subjects .......................................................................................................................... 27
    Stimuli and tasks ............................................................................................................ 27
    Measurements and analyses ......................................................................................... 30
  Results .............................................................................................................................. 34
    Behavioral ...................................................................................................................... 34
    Regions-of-interest analyses ....................................................................................... 34
    Exploratory statistical cluster plots and source modeling ....................................... 36
  Discussion ....................................................................................................................... 37
    Phase I effects (100–200 ms) ....................................................................................... 38
Biological motion in ASD

Phase II effects (200–350 ms)................................................................................40
Phase III effects (400+ ms)..................................................................................43
Conclusion............................................................................................................44
Acknowledgments ...............................................................................................44
Chapter II: Tables and Figures..........................................................................46
Chapter III ..........................................................................................................65
Abstract ..............................................................................................................60
Introduction ..........................................................................................................61
Methods ...............................................................................................................66
Participants .........................................................................................................66
Stimuli and Tasks ...............................................................................................67
Measurements and Analyses ..............................................................................69
  Behavioral analyses ..........................................................................................69
  Electrophysiology ............................................................................................70
  EEG analysis strategy .......................................................................................71
Results ................................................................................................................74
  Behavioral findings ...........................................................................................74
  Electrophysiology .............................................................................................74
  Stage one analysis: GLM of main effects and interactions ................................74
  Stage two analysis: HLM of the group biological motion effect ......................76
Discussion ............................................................................................................77
  Typical electrophysiology of biological motion processes ............................77
  Biological motion processing in the autism spectrum ....................................80
Conclusion ............................................................................................................83
Acknowledgments ...............................................................................................84
Chapter III: Tables and Figures........................................................................86
Chapter IV ........................................................................................................108
CHAPTER I

GENERAL INTRODUCTION
**GENERAL INTRODUCTION**¹

Social processing is a hallmark of human cognition and we are capable of detecting socially salient signals from extremely impoverished sensory information. A prime example is the robust ability to detect diverse social information from so-called biological motion (BM) point light displays (PLDs). In these stimuli, subjects view the motion of a small set of dots configured to the joints of an observed actor as he/she performs common motions (see Johansson, 1973; 1976). Remarkably, from this very sparse sensory information, humans can detect diverse information from gender (e.g. Mather and Murdoch, 1994; and Troje, 2002) to mood (e.g. Atkinson et al., 2007; Pollick et al., 2001; and Pollick et al., 2002). In recent years, considerable effort has gone into trying to understand the neural underpinnings of biological motion processing, in large part because it appears to be disordered in a number of clinical populations such as those with schizophrenia (e.g. Kim et al., 2005) or autism (e.g. Blake et al., 2003).

**POINT-LIGHT DISPLAYS OF BIOLOGICAL MOTION**

The founder of modern BM research was arguably the late Dr. Gunnar Johansson who, in the early 1970’s, attached point-lights to the joints of actors and then analyzed viewer’s abilities to detect and interpret their motion in a dark room. Since, in these displays, the movement of a body is reduced to only the motion of dots that

¹ Portions of this chapter are drawn from Krakowski *et al.*, 2011.
represent the key joints (see figure 1), his finding of a marked ability to discern human action suggested that BM detection is a fundamental and specialized process of the human brain. Since then, behavioral and neural data have continued to demonstrate a profound sensitivity in the brain in similar point-light displays (PLDs) to everything from actions (see e.g. Dittrich, 1993; Bellugi & Lutes-Driscoll, 1981), to intentions (e.g. Runeson and Frykholm, 1983; Sebanz & Shiffrar, 2009), emotions and mood (see e.g. Atkinson et al., 2004; Clarke et al., 2005; Chouchourelou et al., 2006; Dittrich et al., 1993; Dittrich et al., 1996; Pollick et al., 2001), gender (e.g. Cutting and Kozlowski, 1977; Pollick et al., 2005), identity (e.g. Jokisch et al., 2006; Loula et al., 2005) and even sexual orientation (see e.g. Johnson et al., 2007).

In modern BM research, PLDs have to a large degree become synonymous with BM. PLDs essentially eliminate virtually all the static, body-form information, while still yielding a strong social signal from motion cues alone. This is accomplished via both global and local informational components.

**Global** signals include the fixed, rotational relationships of points on the same rigid limb, which are also essential sources of information when processing *inanimate*, rigid point-light objects. More specific to BM are the rhythmic, functional, global motion patterns unique to organisms such as humans such as the symmetry between contralateral arms and legs and opponency between ipsilateral arms and legs while a human walks.

**Local** signals include the characteristic “minimum jerk” trajectories of the *individual* points in a BM PLD. By minimizing jerk through formulaic, smooth
accelerations and decelerations, an animal can locomote rapidly with minimal injury to joint and limb. In a similar vein, local motion information can also include the characteristic accelerations and decelerations associated with an organism functionally overcoming gravity and friction. These motion signals are detectably distinct from e.g. the inanimate and aimless motions of a leaf tossed by the wind or of a raindrop falling from the sky.

The combination of these global and local BM signals provides more than ample information for a neuronal system devoted to detecting the presence of partners, predators, or prey, in the environs of a human or animal. This ability to detect BM is of such prime import to an organism's survival that it is perhaps no surprise that it is both evolutionarily and developmentally early, existing in just-hatched chicks (see e.g. Vallortigara, Regolin, & Marconato 2005), as well as newborn human infants (see e.g. Simion, Regolin, and Bulf, 2008). Nonetheless, modern behavioral, social-cognitive, and perceptual neurosciences are only now beginning to scratch the surface of this sophisticated and fundamental process.

**NEUROANATOMY OF BIOLOGICAL MOTION PROCESSING**

Much recent BM research has focused on localizing the cortical and subcortical brain areas involved in general BM processing (for an excellent review, see Blake and Shiffrar, 2007). Although quite a number of regions have been implicated thus far, the area most prominently associated with BM processes is the posterior superior temporal sulcus (pSTS; see e.g. Bonda et al., 1996; Puce et al., 1998; and Grossman et al.,
Biological motion in ASD

2000; see figure 3), with some evidence suggesting a right-hemisphere bias in pSTS (e.g. Peuskens et al., 2005). This makes a lot of sense when you consider that verbal and nonverbal communication between humans is typically an audiovisual form of BM and that pSTS is an association area that forms the first major convergence between the visual form and motion pathways and also interacts with auditory and language areas, as well as higher order affective and cognitive areas.

Another area often implicated is the nearby extrastriate body area (EBA; see Figure 3), which is also active during the processing of static images of the human body (e.g. Downing et al., 2001 and Taylor et al., 2007). EBA was shown to be more strongly activated for canonical biological motion than for scrambled PLDs (Peelen et al., 2006; see however Grossman and Blake, 2002), although Downing et al. (2006) have suggested that stronger activation of EBA to BM stimuli might simply reflect that EBA is involved in static structural information processing rather than actual “motion dynamics”.

Some debate also surrounds the roles of general motion processing areas, such as the human homolog of the middle temporal gyrus in monkeys (hMT/V5) and the kinetic occipital (KO) region (located posterior and medial to hMT; see Figure 3). For example, a number of studies have reported differential activation of KO for BM stimuli (e.g. Vaina et al., 2001; Santi et al., 2003; and Peuskens et al., 2005). Similarly, Vaina et al. (2001) and Ptito et al. (2003) both found significant BM-related effects in area hMT. In contrast, Grossman and Blake (2002) and Downing et al. (2001) found no significant differences between canonical BM stimuli and their scrambled counterparts in these regions. Perhaps most compellingly, Grossman et al. (2005)
reported that while transcranial magnetic stimulation (TMS) over STS impaired BM perception, it had no effect on BM perception when applied over hMT.

A number of additional form-processing cortical regions have also been implicated, including the fusiform gyrus (FFG) or the occipital face area (OFA; see Figure 3) (e.g. Vaina et al., 2001, Grossman and Blake, 2002 and Michels et al., 2005). Similarly, Vaina et al. (2001) reported activation of the ventral surface of the temporal lobe. Beauchamp et al. (2003) found this activation to be more pronounced for whole body displays than for PLDs. Michels et al. (2005) found that areas traditionally associated with the processing of static human images were differentially activated by different levels of form information in their BM stimuli. In contrast, activation in these areas remained unchanged in response to differing local motion information.

An additional area plausibly responsive to BM stimuli is premotor cortex. Saygin et al. (2004) used fMRI to determine that putative mirror neuron networks in premotor cortex respond to PLDs of human BM. In support, Ulloa and Pineda (2007) found significant suppression of electrophysiological mu rhythms (8–13 Hz) in response to BM PLDs, which they also associated with mirror neuron activity in premotor cortex.

In addition to cortical selectivity, cerebellar activity in response to BM stimuli has also been reported. Grezes et al. (1998) implicated right cerebellum in the visual processing of "meaningful" and "meaningless" actions and Grossman et al. (2000) found cerebellar activity in response to BM stimuli in the anterior portion, starting near the midline. Vaina et al. (2001) found selective activation for BM stimuli in the lateral cerebellum. More recently, Sokolov et al. (2010) reported that patients with left lateral
cerebellar lesions, as opposed to medial lesions, show BM processing deficits. The cerebellum has also previously been associated with visual motion-percept processing (see Gao et al., 1996) as well as with action judgments (e.g. Parsons et al., 1995; but see Grezes et al., 2001).

Overall, there has been a substantial amount of both concurring and conflicting research regarding a diverse network of cortical and subcortical sites distributed across the brain that play a role in BM processing. Since BM is such a fundamental source of dramatically diverse socially salient information, this is hardly surprising. Specifically, BM can be analyzed in early perceptual phases that process basic sensory patterns and dynamics. It can also be analyzed at higher-order levels of processing for specific cognitive and emotional content such as with theory-of-mind (ToM). Unfortunately, however, while the neuroimaging techniques such as fMRI used in the aforementioned studies have a high spatial resolution capable of discerning activation patterns at a millimeter (mm) scale, temporally they provide only a crude snapshot of brain activation, and are thus not ideal for segregating early sensory processes from later cognitive ones. As such, without direct evidence of the physiological processes by which low-level sensory events become a social percept, neuroimaging ultimately provides only a relatively static picture of the areas activated. To fill in this crucial part of the BM narrative, we turn to the temporally-refined methods of electrophysiology.

**NEUROPHYSIOLOGY**

In contrast to the abundant and ever-growing body of work regarding the
localization of BM processes, there is relatively little consistent data regarding the precise timing of events across this network of implicated regions. Such information is valuable with regard to understanding feedback and feed-forward connections between STS and putative mirror neuron networks in premotor cortex and higher associated social cognition areas such as orbitofrontal cortex and the amygdala (see e.g. Gallagher and Frith, 2003 and Stone et al., 2003).

ELECTROENCEPHALOGRAPHY

Perhaps the most useful tool for the spatiotemporal analysis of neuronal events in the human brain is the electroencephalogram (EEG). Since its initial discovery by Hans Berger in 1924, EEG has become a powerful tool both in exploring typical brain function, as well as in clinical diagnoses. EEG measures electric potential fluctuations on the scalp that are caused by the synchronous firing of large numbers of similarly oriented neurons in the brain (see Luck, 2005). With the advent of modern computers, new more sophisticated techniques emerged, such as the recording of event related potentials (ERPs), which are detected by averaging together scalp responses time-locked to a given stimulus.

As opposed to neuroimaging techniques, EEG directly monitors brain activity, thereby providing a much higher temporal resolution of neuronal events (milliseconds [ms] rather than seconds). In addition, it can be implemented in a manner less likely to cause the symptoms of claustrophobia that can be associated with other modern techniques such as fMRI and MEG (see e.g. Murphy and Brunberg, 1997). As such, it is particularly useful with vulnerable, clinical and/or young populations. Normal ERPs
tend to have predictable, sequential, positive and negative components which are typically labeled based on their polarity and timing (e.g. P300 for a positive component at 300 ms or N1 for the first negative component after ERP-onset).

Using ERPs, Hirai et al. (2003) reported a significant right occipito-temporal amplification of an “N200” component in response to BM stimuli, as well as a bilaterally amplified “N240”. Similarly, Hirai et al. (2005) observed a later “N200” for BM stimuli when they were masked by additional, scattered, slowly moving dots. Jokisch et al. (2005) found amplifications of the negative event-related potential (ERP) components at 180 ms (N1) and 230–360 ms (N2) for biological motion PLDs relative to their scrambled counterparts. They also reported that the N1 and N2 effects were greatest before their respective components peak. Using inverse source localization methods (LORETA-analysis), they suggested that generators of the N1-effect were based in the posterior cingulate gyrus and in the left lingual gyrus and that the N2-effect arose from sources in the right fusiform gyrus (FFG), right superior temporal gyrus, as well as in the orbitofrontal cortex. There is, however, ample room for skepticism regarding these results due to the low spatial resolution used in the recording (30 electrodes).

In a later study, Hirai and Hiraki (2006a) reported a significantly greater negativity in the 0–100 ms time-window for their scrambled condition vs. their normal BM PLDs, while the converse was true regarding the 200–300, 300–400, and 400–500 ms time-windows. Also, they reported no significant BM effects in the 100–200 ms N1 time-window. In a recent experiment involving both children and adults, Hirai et al. (2009) found main effects of larger and later bilateral N1 peaks, larger bilateral N2s, as well as larger amplitudes between the peaks, for BM relative to scrambled motion (SM),
over occipito-temporal sites. The reason for the inconsistencies between these findings remains unclear, though perhaps it is partly explained by the atypical time-windows used in the Hirai and Hiraki (2006a) study.

MAGNETOENCEPHALOGRAPHY

In addition to EEG, another technique useful for measuring the timing of neuronal events is magnetoencephalography (MEG) which measures modulations of the magnetic fields associated with neuronal electric currents. Using MEG, Pavlova et al. (2004) concentrated on responses in the frequency domain, finding enhanced responses between 25 and 30 Hz (“gamma”), as early as 100 ms for both upright and inverted BM PLDs over left occipital cortex, with additional effects for upright PLDs over parietal and right temporal cortices at 130 and 170 ms, respectively. Scrambled displays did not affect “gamma” responses. In a more recent study, Pavlova et al. (2006) found these effects as early as 80 ms over left parieto-occipital cortex. They also reported right-hemisphere effects due to attention to BM stimuli at 120 ms over parietal cortex and at 155 ms over temporal cortex (see next section). Also using MEG, Virji-Babul et al. (2007) recorded significantly increased oscillatory responses between 15 and 35 Hz over the left posterior temporal area at between 250 and 350 ms when subjects viewed PLDs of human motion, which was not found in response to PLDs of object motion.

In sum, these twin techniques of EEG and MEG present a framework to map out the different stages of BM processing from a low-level percept to a complex social construct. In what follows, we will explore the roles of two relevant aspects of these processes, namely, display orientation and attention.
**DISPLAY ORIENTATION AND BIOLOGICAL MOTION PROCESSING**

One of the most important areas of research in cognitive neuroscience today is the interpretation of low-level sensory data into a higher-order cognitive “object”. A major topic in this area is how the orientation of a visual stimulus plays a direct role in its perception as a coherent whole. This has been most often shown in simple, static form processing such as the well-documented face “inversion effect”, where e.g. an inverted face is more difficult to identify. However, inversion effects have also been demonstrated using dynamic BM PLDs. For example, newborns have been shown to prefer upright vs. inverted walking “chicken” PLDs (Simion, Regolin, and Bulf, 2008).

In direction-discrimination tasks, a major contributor to the BM inversion effect appears to be related to the detected accelerations of the feet (Chang and Troje, 2009). In that study, participants were able to correctly identify the direction of a scrambled point-light walker (PLW) provided the dot-trajectories representing the motion of the feet remained upright. Shipley (2003) has demonstrated that this effect appears to be based on the spatiotemporal dynamics of the display, i.e. foot motion trajectories across species reflect a particular pattern in response to gravity and thus their correct visual interpretation relies directly on the orientation of the display. It seems quite plausible, however, that this finding is substantially limited by the fact that the detection of walking direction is an aspect of BM-processing that is substantially dependent on the interaction of the feet with the impermeable ground and gravity. As such, this effect likely has less influence regarding other BM signals such as upper body motion.
The brain processes underlying the BM inversion effect have also begun to be explored. Using EEG to monitor brain activity in adults, Stekelenburg and de Gelder (2004) reported an amplification and delay of the electrophysiological ‘N170’ components over parietal sites in response to the inversion of viewed static bodies relative to upright. They interpret this finding as indicative of early socially-salient structural encoding in fusiform cortices. Using neuroimaging, Grossman and Blake (2001) have found that while inverted BM (IM) displays activated the posterior superior temporal sulcus (pSTS) more than did scrambled motion (SM), the response was weaker than for upright BM.

**ATTENTION AND BIOLOGICAL MOTION**

Another major aspect of cognitive processing is the role of explicit attention. With regard to BM, early research supported spontaneous, early, feed-forward BM-processing models (e.g. Johansson, 1973; and Mather et al., 1992) where the process was automatic and disregarded the subject’s cognitive state or intention. More recent studies, however, have also implicated the role of feedback attentional processes in the perception of biological motion. For example, Cavanagh, Labianca, and Thornton (2001) found that attentional load delayed detection of an oddball PLD. Similarly, Thornton, Rensink, and Shiffrar (2002) demonstrated the need for focused attention to detect biological motion under certain noisy conditions (see next section).

Current brain research also demonstrates a more direct role of attentional processes in the perception of BM. In a recent, combined fMRI/EEG study, Safford et al. (2010) used a “double-exposure” paradigm in which either tool motion (TM) and BM,
TM and SM, or BM and SM overlaid each other and subjects attended either TM or BM. Attention to TM suppressed the BOLD response of the right STS/medial temporal gyrus (MTG), while attention to BM suppressed the BOLD response of the left inferior temporal sulcus (ITS)/MTG. Additionally, category-based cortical current source density modulations began relatively late (after ~ 450 ms), probably in large part because of the subtle nature of the stimuli. It should be noted however that the ostensibly non-BM control stimulus of TM displays similar motion trajectories as its driving, biological muscular activity (e.g. minimum jerk), and is therefore arguably also a form of BM (see e.g. Maravita and Iriki, 2004), somewhat limiting the interpretation of their results in the context of other BM paradigms.

Using electrophysiology, Hirai et al. (2005) found significant amplification of the N330 component when subjects attended BM stimuli rather than concurrently-presented geometric stimuli (see also Hirai and Hiraki, 2006b). Also, as mentioned earlier, Pavlova et al. (2006) found MEG effects in the gamma response as early as 80 ms for both attended and unattended tasks. However, only their attended biological motion stimuli produced results over right cortices parietally at 120 ms and temporally at 155 ms. In addition, both attended stimuli yielded effects frontotemporally at 180–200 ms, a result they suggested implicated working memory.

**THE EMERGING PICTURE**

While the results of much of the research are still not entirely consistent, a general model of BM processing does appear to emerge. Low level, feed-forward systems play a prominent role, particularly when the stimuli are presented in non-noisy
conditions and at short interstimulus intervals (ISI) (see Mather et al., 1992). Yet BM can still be perceived when presented at display rates faster than those usually associated with low-level, local motion processes (Thornton, 1998). Thornton et al. (2002) reported that while attention was necessary to perceive BM in “dynamic noise” (see Thornton et al., 2002) at long ISIs, short ISIs yield a BM percept even in the absence of attention (see also Thornton & Vuong, 2004). As such, both top–down and bottom–up processes likely play a role in BM perception, with attention playing a greater role in integrating BM information that cannot simply be processed automatically.

Similarly, and as evidenced by the aforementioned neuroimaging studies, both motion and form processes appear to interact dynamically in BM detection and perception (see e.g. Beintema & Lappe, 2002; and Pinto & Shiffrar, 1999). Basing themselves on the physiological and neuroimaging data, Giese and Poggio (2003) formulated a feed-forward model of parallel ventral-form and dorsal-motion processes that analyze “snapshots” of human forms and “optic-flow” (OF) patterns, in an increasingly global manner, as they converge toward STS and associated areas (see also Peuskens et al., 2005). According to this feed-forward model, BM processing involves the two visual pathways. Motion information traverses dorsally from local motion detectors in V1 to V2 and hMT. It then ascends to local OF pattern-detectors in hMT, MST, and/or KO. The information is then further processed by complex OF-pattern detecting neurons in STS and/or FA, as well as by motion pattern neurons in STS, FA, and/or ventro-lateral premotor cortex. Form information is conveyed ventrally from simple (and complex) cells in V1 and V2 to complex cells in V4. View-tuned snapshot neurons in inferotemporal cortex, EBA, STS, and/or FA further process the
information before relaying it to the motion pattern neurons of STS, FA, and/or F5, where it can be integrated with dorsally-processed information. In Chapter 2, we use high-density EEG to map out the neurodynamics of BM processing. We identify the onset and offset of major processes as well as their susceptibility to the “top-down” manipulation of attention. As such, we also lay the groundwork for our exploration of the development of these processes and their implication in autism in Chapter 3.

THE TYPICAL DEVELOPMENT OF BIOLOGICAL MOTION PROCESSES

The behavioral literature to date demonstrates that sensitivity to upright BM PLDs is apparent as early as two days old (Simion, Regolin, and Bulf, 2008), with overall accuracy approaching adult levels as soon as five years of age (Pavlova et al., 2001, Blake et al., 2003) though response times (RTs), as well as subtler BM-related processes likely differ substantially. In school-age children (7-14 years), Hirai et al. (2009) reported an earlier electrophysiological P1-component as well as amplified N1 and N2 over occipitotemporal sites in response to BM vs. SM. Lepage and Théoret (2006) found that mu rhythms (8-13 Hz) are attenuated in children under 11 during the observation and execution of hand movements, with greater effects for goal/object-oriented motion (similar to adult findings). They also found theta effects (3.5-7.5 Hz) for

---

2 This section and the following, “Biological motion processing in the autism spectrum”, also appear, in modified form, in chapter III.
the observation of hand motion.

With respect to attention and development, at the time of writing there does not appear to be any literature specific to biological motion processing. However, overall developmental neurocognitive research to date suggests that the younger brain is less likely to show as much attentional effects in that cognitive functioning in general and attentional suppression in particular are late processes to mature (see e.g. Casey, Galvan, and Hare, 2005). Similarly, we might expect that activation patterns are more discriminatory and localized as the brain matures (see e.g. Durston and Casey, 2000; Johnson, 2011).

**BIOLOGICAL MOTION PROCESSING IN THE AUTISM SPECTRUM**

Symptoms of the autism spectrum disorders (ASD) include difficulties with interacting socially and with reciprocal communication, as well as lower level sensory deficits (see e.g. Watling, Deitz, and White, 2001). There is substantial controversy in the behavioral literature as to whether BM-processing deficits are also implicated in ASD. Using a free-response labeling task, Moore, Hobson, and Lee (1997) reported a significant impairment in emotional and mental-state interpretation of BM PLDs, but not in overt BM action-categorization, in autistic children (cASD) and adolescents. Similarly, Hubert *et al.* (2007), in a study of high-functioning young adults (21±6 years), also found only a significant impairment in detecting emotion from BM PLDs. Parron *et al.* (2008) found no effect for BM processing, *per se*, instead reporting deficits specific to the detection of emotion from BM PLDs in subjects with ASD (age = 11±3 years), more consistent with an emotion-processing dysfunction than a general BM-processing
disorder. Similarly, Saygin, Cooke, and Blakemore (2010) reported comparable psychophysical thresholds for BM detection in noise in adults with ASD. More recently, Rutherford and Troje (2011) found no difference between autistic adults and typical controls in the perception of BM, instead reporting a significant correlation between BM perception and IQ in the participants with ASD.

In contrast to these findings of no BM-specific dysfunction, Blake et al. (2003) reported that d’ scores in a simple BM-categorization task were significantly lower in cASD than in mental-age matched TDs, and were also correlated with the severity of the disorder. Similarly, Annaz et al. (2010) reported that for children of 5-12 years, while TDs steadily improve in perceptual sensitivity to BM (as measured by d’ scores), cASD showed a flat developmental trajectory, overlapping with TDs only at the youngest age. Koldewyn, Whitney, and Rivera (2010) also reported higher thresholds for detecting BM in noise amongst adolescents with ASD. Similarly, Atkinson (2009) found that when participants were forced to choose action-labels from a list, adults with ASD did exhibit a BM PLD processing deficit. They also reported a significant correlation between emotion detection and motion coherence processing. Kaiser et al. (2010b) suggested that while those with ASD are able to process BM, they lack the typical enhancement of visual sensitivity to BM relative to object motion. This may well be a result of early attentional differences in very young children with ASD who do not preferentially attend to BM (Klin and Jones, 2008; Klin et al. 2009; Annaz et al. 2011).

Ultimately, recent neuroimaging findings do indeed point to affected BM-processing in ASD. Herrington et al. (2007) reported that while Asperger’s patients and typical adults reached ceiling levels on direction discrimination from BM PLDs,
there was less activity in superior temporal areas during these tasks, suggesting the possible recruitment of alternative neural pathways. Freitag et al. (2008) reported that adolescents and adults with ASD had longer response times in categorizing coherent BM (CM) and scrambled motion (SM), as well as significantly reduced activity in parietal and temporal areas. Koldewyn, Whitney, and Rivera (2011) found that adolescents with ASD had reduced activity in posterior superior temporal sulci (pSTS), parietal, and frontal cortices relative to controls in a BM-in-noise direction discrimination task, with dorsolateral prefrontal activity negatively correlated with symptom severity. Most recently, McKay et al. (2011) conducted an fMRI study of adults with ASD and typical controls matched for age and IQ. Behaviorally, participants with ASD demonstrated thresholds similar to controls for detecting the direction of partially scrambled point-light walkers. However, the fMRI activation patterns of those with ASD suggested two distinct form and motion networks, in place of the temporal-to-parietal activation seen in the controls (see McKay et al., 2011). Zilbovicius et al. (2006) suggest that early STS dysfunction in ASD may be a “first-step” in the etiology of the disorders. (See also Pelphrey and Carter, 2008a and Pelphrey and Carter 2008b).

Because imaging techniques have low temporal resolution, they are not very reliable at revealing whether apparent neurophysiological differences reflect dysfunctions of early, perceptual stages of BM processing in the disorders, or only of later, higher-cognitive stages of processing. As already discussed, the most direct way to resolve this question is through the use of EEG which provides precise timing of potentially implicated pathways and effects. As such, the experiments in chapter III explore the typical and atypical development of these processes as the spatiotemporal
neural dynamics of biological motion processing are mapped out in ASD and in typically developing controls using high density EEG.
CHAPTER I: TABLES AND FIGURES
**Figure 1:** A single frame of a point-light display of a human walking.
Figure 2: Hans Berger (1873–1941) and the “electro-encephalogram” (circa 1920).
Figure 3: Approximate sites of candidate areas activated by BM. (pSTS = posterior superior temporal sulcus, hMT = human homolog to monkey medial temporal area, EBA = extrastriate body area, KO = kinetic occipital area, OFA = occipital face area, FBA = fusiform body area; Note: EBA heavily overlaps with hMT. Modified from: Patrick J. Lynch, medical illustrator; C. Carl Jaffe, MD, cardiologist. 
http://creativecommons.org/licenses/by/2.5/)
CHAPTER II

THE NEUROPHYSIOLOGY OF HUMAN BIOLOGICAL MOTION PROCESSING: A HIGH-DENSITY ELECTRICAL MAPPING STUDY

This chapter is drawn from Krakowski et al., 2011.
ABSTRACT

The neural processing of biological motion (BM) is of profound experimental interest since it is often through the movement of another that we interpret their immediate intentions. Neuroimaging points to a specialized cortical network for processing biological motion. Here, high-density electrical mapping and source-analysis techniques were employed to interrogate the timing of information processing across this network. Participants viewed point-light-displays depicting standard body movements (e.g. jumping), while event-related potentials (ERPs) were recorded and compared to ERPs to scrambled motion control stimuli. In a pair of experiments, three major phases of BM-specific processing were identified: 1) The earliest phase of BM-sensitive modulation was characterized by a positive shift of the ERP between 100 and 200 ms after stimulus onset. This modulation was observed exclusively over the right hemisphere and source-analysis suggested a likely generator in close proximity to regions associated with general motion processing (KO/hMT). 2) The second phase of BM-sensitivity occurred from 200 to 350 ms, characterized by a robust negative-going ERP modulation over posterior middle temporal regions bilaterally. Source-analysis pointed to bilateral generators at or near the posterior superior temporal sulcus (STS). 3) A third phase of processing was evident only in our second experiment, where participants actively attended the BM aspect of the stimuli, and was manifest as a centro-parietal positive ERP deflection, likely related to later cognitive processes. These results point to very early sensory registration of biological motion, and highlight the interactive role of the posterior STS in analyzing the movements of other living organisms.
**INTRODUCTION**

Humans, and indeed all creatures, have a need to rapidly detect and process sensory percepts that suggest the presence of another living organism. Perhaps one of the richest sources of such information comes through visual processing of the movements of others, commonly known as “biological motion” (BM). In recent years, considerable effort has gone into trying to understand the neural underpinnings of biological motion processing, in large part because it appears to be disordered in a number of clinical populations such as those with schizophrenia (e.g. Kim et al., 2005) or autism (e.g. Blake et al., 2003; See, however, Freitag et al., 2008 and Parron et al., 2008). Behavioral and neuroimaging data have demonstrated, at least in humans, a profound sensitivity to everything from gender (e.g. Mather and Murdoch, 1994 and Troje, 2002) to mood (e.g. Atkinson et al., 2007, Pollick et al., 2001 and Pollick et al., 2002), even in cases of highly impoverished information, such as those using Johansson's (1973) point-light displays (PLDs). In these displays, the movement of a body is reduced to the motion of dots that represent the key joints. The purpose of the current study was to use high-density electrical mapping to assess the relative timing of BM processing, and to assess the role of attention in this processing.

In the current study, we implement two basic BM tasks to more fully corroborate and clarify the electrophysiological spatiotemporal processing of biological motion stimuli. We use high-density electrode arrays (168 channels) to aid in localization analyses. In contrast to previous electrophysiological studies which focused on just two components, our analyses explore effects both at component peaks as well as between them. A clearer picture of the actual timing of BM processes will enable a clearer
understanding of how the different brain areas involved in BM processing interact. As of yet there appears to be no EEG literature addressing precisely when BM processing begins. Such information is valuable in more accurately evaluating potential feed-forward–feedback flow in BM processes and social cognition. Along these lines, we also explore the differences in attended vs. unattended tasks as manifested in our electroencephalographic data. In doing so, our intention is to establish a baseline for comparison with clinical populations.

**MATERIALS AND METHODS**

**SUBJECTS**

Fourteen (4 female) volunteers (mean age = 28.6 years.; SD = 5 years), with no reported neurological impairments, participated in this study. All subjects provided written informed consent after the procedures of the experiment were fully explained to them, and all procedures were approved by the Institutional Review Boards of the Nathan Kline Institute and the City University of New York. All subjects received a modest fee for their participation.

**STIMULI AND TASKS**

Displays were presented on either an 18” Ilama Pro VisionMaster 502 (nine subjects) or a 30 × 40 cm MultiSync FE2111SB (five subjects) monitor controlled by Presentation™ software. All experiments were conducted in a sound-attenuated electrically shielded room illuminated only by light from the video screen. In both tasks, all stimuli appeared black against a white background. Subjects were instructed to maintain fixation on a central fixation-cross and eye-position was monitored by vertical
and horizontal electro-occulogram.

Video-clips of an adult human engaged in common activities (e.g. running, kicking, climbing, throwing, and jumping) were imported to a computer to create the biological motion stimuli. Markers were placed on the actor's joints in each frame of the sequence, such that the final clips were only composed of up to seven moving dots (i.e. point-light displays). Scrambled motion (SM) sequences were created from the normal biological animations and consisted of the same individual dots undergoing the same local motions as the biological counterparts. Scrambling was produced by randomizing the temporal phases and spatial locations of the dots in a given animation, thereby skewing the hierarchical, pendular motions that are characteristic of biological motion (see Figure 1). The methodology behind the generation of biological motion sequences is discussed more fully in Grossman and Blake, 1999 and Blake et al., 2003.

The experiment consisted of two tasks in each of which subjects were presented with six or seven five-minute blocks of randomized, repeating video-clips, with 110 clip-presentations per block (55 BM + 55 SM; total time = ~ 35 min per task). In total, twenty distinct video-clips were used, ten of which represented point-light displays of canonical biological motion (see below), and ten of which were scrambled images thereof. These twenty clips were selected from a larger pool of 100 clips to match for retinal displacement (see Supplementary Materials). Each clip was composed of 29 frames presented at the monitor refresh-rate of 60 Hz. Inter-stimulus interval was randomized between 500 and 1000 ms.

In the first task, in random clips (nine percent of total clips), one of the dots would
briefly turn red. Only a single dot changed color on these target trials, the position of which within the moving object was randomized, and this only occurred after the movement clips had already begun, never beginning before frame 4 (i.e. 54 ms after onset). The duration of the color-change was then very brief, lasting just 4 or 5 frames (67–83 ms). The onset of the color-change was also randomized such that it could appear at any time from frame 4 to frame 23 (383 ms). As such, participants needed to attend across the entire stimulus presentation period to rule out target presence. Subjects were instructed to respond to these “target” clips by depressing a mouse key. Subjects were not explicitly informed that some of the clips portrayed human motion, although this was immediately obvious to subjects upon debriefing. Subjects were also instructed to delay their responses until the completion of each video-clip in order to diminish the impact of motor response-related artifacts. Target-trials were excluded from later analysis enabling a contrast between non-target BM and non-target SM without additional motor response artifacts or target-related processing effects.

In the second task, subjects were once again presented with the same video-clips (minus the red-dot target clips of the first task). This time, however, subjects were asked to judge whether the clips depicted human motion or scrambled motion. Following each trial, the subject indicated whether or not the animated dots portrayed “human” activity by pressing one of two pre-assigned computer keys. A forced-choice paradigm was used to control for target-effects. As such, differences in the response would reflect the difference between attended target BM and attended target SM, and not motor planning or inhibition. The second task always followed completion of the first task to maintain presumed naïveté in the first task regarding the presence of BM in the
displays.

Over the course of both tasks, subjects were encouraged to take breaks between blocks whenever they deemed it necessary, in order to maintain high concentration and reduce fatigue.

**MEASUREMENTS AND ANALYSES**

Continuous EEG was acquired through the ActiveTwo BioSemi™ electrode system from 168 scalp electrodes, digitized at 512 Hz. For display purposes, data were filtered with a low-pass 0-phase shift 96 dB 40 Hz filter after acquisition. With the BioSemi™ system, every electrode or combination of electrodes can be assigned as the reference, which can be done offline. BioSemi™ replaces the ground electrodes used in conventional systems with two separate electrodes: Common Mode Sense (CMS) active electrode and Driven Right Leg (DRL) passive electrode. These two electrodes form a feedback loop, rendering them references. For a detailed description of the referencing and grounding conventions used by the BioSemi™ active electrode system, visit [www.biosemi.com/faq/cms&drl.htm](http://www.biosemi.com/faq/cms&drl.htm).

After acquisition, data were re-referenced to a medial-frontal site (FPz) for analysis. After each recording session, and before the electrode cap was removed from the subject's head, the 3D coordinates of all 168 electrodes with reference to anatomic landmarks on the head (nasion and preauricular notches) were digitized with a Polhemus Magnetic 3D digitizer. Data were analyzed and artifacts were rejected offline using BESA™ multimodal neuroimaging analysis software package (MEGIS Software GmbH, Munich, Germany). Because of the relatively long duration of each video-
stimulus, artifacts were only rejected before 600 ms. Accepted trials were epoched (100 ms prestimulus to 1300 ms post-stimulus) and then averaged separately for each condition. To control for low-level stimulus properties, only non-target trials were included in the averages for the color-detection task. We defined baseline as the mean voltage over −50 ms to 0 ms preceding the onset of the stimulus. Trials with blinks and large eye movements were rejected offline on the basis of horizontal and vertical electro-oculogram recordings. An artifact rejection criterion of 80–100 μV was used at all other electrode sites to exclude periods of high EMG and other noise transients. From the remaining artifact-free trials, we computed averages for each subject.

Analysis strategy

Because there is little consistent literature regarding the precise timing of the electrophysiological response to BM stimuli, we took a two-stage approach to our statistical analyses. The first stage was a simple three-way ANOVA (factors: Task: attended/unattended; Hemisphere: left/right; and Motion: BM/SM) based on the findings of past studies. The second stage comprised a more comprehensive analysis of all time-points and sites to more fully explore the scalp effects in response to the two tasks. What follows is a brief description of these two analyses. See also Wylie et al. (2003), who employed a similar methodology.

Stage one analysis: regions-of-interest and ERP components

For our initial analysis, and basing ourselves on findings in the previous literature (e.g. Hirai et al., 2003 and Jokisch et al., 2005), we defined bilateral regions-of-interest comprising three adjacent electrode sites on or near the temporo-parieto-occipital junctions bilaterally, roughly corresponding to underlying higher order visual processing
areas such as STS. We then generated waveforms averaged from each set of three electrodes. Componentry was defined based on waveforms collapsed across both canonical BM and scrambled conditions (see Figure 2), i.e. unbiased by observation of any possible effects.

Waveforms were largely similar to those reported in the aforementioned literature (e.g. Jokisch et al., 2005 and Hirai et al., 2003) with higher-frequency, large-amplitude P110 and N180, as well as lower-frequency, lower amplitude P280 and N360. The area under each curve (AUC) was computed for seven consecutive time-windows. For the sharper P1 and N1 components, 20 ms time-windows centered at the peaks were computed. In addition, and based on the aforementioned findings in the EEG and MEG literature (e.g. Jokisch et al., 2005, Hirai and Hiraki, 2006a, Pavlova et al., 2004 and Pavlova et al., 2006), we also looked at the 20 ms time-window before the P1 peak (“eP1”), between the P1 and N1 peaks (“P1–N1”), and in the post-peak, late N1 (“N1–P2”). For the later, low-frequency components, we computed the consecutive 80 ms time-windows that spanned the components (“P2” and “N2”) (see Figure 2). We conducted a three-way repeated-measures ANOVA with factors of task-type (attend BM vs. unattended), hemisphere (right vs. left), and motion type (BM vs. SM). One subject was excluded from this analysis due to the fact that the second task had been executed with a GoNoGo paradigm, rather than as the forced-choice paradigm used by the remaining subjects. Our critical value was set at α = 0.05.

**Stage 2 analysis. Exploratory statistical cluster plots and source modeling**

In order to incorporate more fully the wealth of information provided by our high-density electrophysiological dataset, we also computed statistical cluster plots for each
task (see Molholm et al., 2002). These maps were created using pointwise, paired, two-tailed t-tests between the VEP responses to our two conditions (BM and SM). As such, we can assess more fully an approximation of the entire differential activation between the conditions across the 500 ms post-stimulus-onset epoch. Since the potential for a Type I error is high with such an approach due to the high number of statistical comparisons, we restrict our analysis to an alpha criterion of 0.01 and, additionally, only accept as significant those data that reach this threshold for 11 consecutive time-points (> 20 ms at our 500 Hz sampling rate; See e.g. Guthrie and Buchwald, 1991 and Foxe and Simpson, 2002, for similar approaches).

Using these statistical cluster plots as a framework, dipole source analyses were then implemented using the BESA software suite (version 5.0.4) to estimate the intracranial generators underlying the spatio-temporally discrete effects. BESA models the best-fit location and orientation of multiple intracranial dipole generator configurations to produce the waveforms observed at the scalp, using iterative adjustments to reduce the residual variance between the solution and the observed data (see e.g. Scherg and Von Cramon, 1985). For the purpose of the modeling, an idealized three-shell spherical head model with a radius of 85 mm and scalp and skull thickness of 6 mm and 7 mm was assumed. The upper bound of the number of modeled dipole sources was determined using an unconstrained test dipole (see Scherg and Picton, 1991). When the number of modeled sources, $m$, is sufficient, addition of another source (test dipole) and solving for $m + 1$ sources would not be expected to further reduce the residual variance, above that attributable to noise. Similarly, when scalp effects appeared to be bilaterally symmetric, dipoles were
constrained for symmetry, provided unconstrained sources were unable to reduce residual variance beyond that attributable to noise. In order to maintain a high signal-to-noise ratio, as well as to generalize our results across subjects, group-averaged VEP data were used. It is worth mentioning that as the modeled equivalent current-dipole represent simplifications of activity in the area, they should be considered as indicators of centers-of-gravity and not necessarily distinct neural sites.

RESULTS

BEHAVIORAL

Hit rates for the first, color-detection task were 91.7% (S.D. = 0.08), with false alarm rates at 11% (S.D. = 0.01). Similarly, in the second, motion-categorization task, accuracy was 92.4% (S.D. = 0.08).

REGIONS-OF-INTEREST ANALYSES

To more clearly demonstrate the overall distribution of the electrophysiological response, VEPs from key scalp sites are shown in Figure 3. Our initial analysis focused on the areas corresponding to PO7 and PO8 in the diagram. As can be seen from the figure, BM generated greater positivity than SM over the right parieto-occipital site from the peak of P1 (~ 110 ms) and continuing toward the N1 peak (~ 180 ms), at which point BM generated greater negativity than SM for upwards of 150 ms. This later effect appeared to have a greater amplitude when BM is explicitly attended, as well as a later offset.

In what follows, we will step systematically through our predefined componentry, analyzing each in their turn (eP1, P1, P1–N1, N1, P2, and N2).
Our analysis of the earliest time-window ('eP1' = 80–100 ms) yielded no significant main effects nor significant interactions.

P1 (100–120 ms) had a significant interaction between hemisphere and motion ($F_{(1,12)} = 5.38; p = 0.04$) with increased amplitudes in right scalp sites in response to BM vs. SM. (See Supplementary Materials with regard to potential confounds regarding this early effect.)

The time-window between P1 and N1 ('P1–N1' = 120–170 ms) had a significant main effect for motion type ($F_{(1,12)} = 10.00; p = 0.01$) as well as a significant interaction between motion and hemisphere ($F_{(1,12)} = 10.10; p = 0.01$). Post-hoc analyses indicated that this was due to a greater negativity over the right hemisphere in response to BM, as well as a reduced negativity in the left.

N1 (170–190 ms) yielded a significant interaction between task-type and hemisphere ($F_{(1,12)} = 5.52; p = 0.04$) with bilateral amplifications of the negativity in response to “attended” BM. N1 approached significance for the main effect of hemisphere ($F_{(1,12)} = 3.93; p = 0.07$), as well as for the interaction between hemisphere and motion ($F_{(1,12)} = 4.07; p = 0.07$).

The time-window between N1 and P2 ('N1–P2' = 190–240 ms) had a significant main effect of task ($F_{(1,12)} = 6.12; p = 0.03$), a significant main effect of motion ($F_{(1,12)} = 20.60; p = 0.001$), as well as significant two-way interactions between task and hemisphere ($F_{(1,12)} = 8.44; p = 0.01$), and task and motion ($F_{(1,12)} = 10.76; p = 0.01$). Post-hoc tests revealed a bilateral amplified negativity for the attended task, an amplified negativity in response to BM, as well as a greater task-related effect in the left.
hemisphere. The difference between BM and SM was greater for the attended task.

Similarly, the P2 (240–320 ms) showed a significant effect for task ($F_{(1,12)} = 5.47; p = 0.04$) and motion ($F_{(1,12)} = 17.24; p = 0.001$), as well as for the interaction between the two ($F_{(1,12)} = 6.66; p = 0.02$). Post-hoc tests revealed a bilateral amplified negativity for the attended task as well as an amplified negativity in response to BM.

The N2 (320–400 ms) had a significant main effect of motion type ($F_{(1,12)} = 6.90; p = 0.02$), as well as a significant interaction between motion and hemisphere ($F_{(1,12)} = 7.32; p = 0.02$). Post-hoc analyses demonstrated that the response to BM after N1 was more negative particularly in the attended task as well as in the left hemisphere (see Table 1).

**EXPLORATORY STATISTICAL CLUSTER PLOTS AND SOURCE MODELING**

As described earlier, we also conducted statistical cluster plots for each task to measure for the effects between the two stimulus-classes (BM vs. SM) (see Figure 5). Our plots over all electrodes and for all time-points showed the most significant effects for the unattended task in the 120–160 ms time-window over parieto-occipital (PO), parietal, and central areas, and at around 200 ms in occipital and PO areas (Figure 5A). In the attended task, our probability maps showed effects which were fairly similar to those in our unattended task for the 100–200 ms time-window (see Figure 5B). In addition, we saw prolonged effects from 200 ms to 350 ms over parieto-occipital areas and from 400 ms onward over parietal and central areas, presumably related to
attentional amplification.

We then estimated the intracranial generators of the scalp electrophysiology seen in the cluster plots with dipole source analyses using the BESA software suite (see earlier in Methods). The early effect in both tasks appeared as a greater positivity over the right occipito-parietal area from 120 to 160 ms. A single dipole over that time period localized at Talairach coordinates: $x = 35$, $y = -69$, and $z = -2$, accounted for 91% of the scalp electrophysiological variance for the unattended task (Figure 6A). For the attended task over that time period, a dipole localized at Talairach coordinates: $x = 23$, $y = -80$ and $z = 20$, accounted for 81% of the variance (Figure 6C).

The second major effect occurred over what appeared to be approximately symmetric sites over the bilateral occipito-temporal cortices from ~200 to 350 ms. Two symmetrically-constrained dipoles at Talairach coordinates: $x = \pm 40$, $y = -69$, and $z = 13$, accounted for 80% of the scalp variance, for the unattended task (Figure 6B). Similarly, we obtained Talairach coordinates of: $x = \pm 40$, $y = -65$ and $z = 7$, which accounted for 89% of the variance, for the attended task (Figure 6D).

The third, attention-related effect (400–500 ms) yielded sources at: $x = -37$, $y = -76$, $z = 16$; $x = 32$, $y = -77$, $z = 10$, which accounted for 93% of the scalp variance in that time-window (Figure 6E).

**DISCUSSION**

In the two experiments reported here, we sought to provide a comprehensive picture of the spatiotemporal dynamics of biological motion processing and their modulation by attention. The use of high-density electrode arrays allowed for a detailed
characterization of evoked responses over time and a more precise estimation of their
cortical sources. It was found that biological motion affected neural processing as early
as ~100 ms after the onset of the first frame of stimulation (see Supplementary
Materials), with robust modulation of the ongoing response thereafter that continued
past 320 ms, irrespective of whether participants specifically attended to the motion
aspect of the stimuli or not. We identified three distinct phases of modulation and we
will treat of each of them in their turn in what follows.

**Phase I Effects (100–200 ms)**

The earliest phase of this BM-sensitive modulation was characterized by a
positive shift of the ERP in the BM condition in the time-window between 100 and
200 ms after stimulus onset. The timing and topographical distribution of this effect is in
relatively close correspondence to early occipital P1 modulations reported by Hirai et al.
(2009) and perhaps with the early onset of differences in gamma band oscillations
found by Pavlova et al., 2004 and Pavlova et al., 2006. This would seem to suggest that
the brain detects BM very early, since the timing of the onset of this effect is such that
no more than the first three frames of the animation (~30 ms each) could realistically
have been registered in cortex before the modulation emerged (see Foxe and Simpson,
2002). Source localization of this activity suggested a likely cortical generator in the
dorsal visual processing stream, in close proximity to regions associated with general
motion processing (KO/hMT) (see Figure 7). Significantly, this modulation was observed
exclusively over the right hemisphere suggesting that right hemispheric neural networks
underlying general motion processing may be specialized for early detection of BM. This
effect is also consistent with the well-established role of right hemisphere temporo-
parietal regions in so-called global processing (e.g. Robertson et al., 1988, and Fink et al., 1997a; see, however, Fink et al., 1997b), since a major aspect of processing the point-light-display stimuli used here lies in constructing a global percept from the coordinated movements of an array of local disconnected elements.

In order to elucidate the effects of attention on BM processing, we conducted Experiment 1 with naive subjects who were instructed to respond to a simple non-BM-related cue (briefly appearing dot-color changes), while in Experiment 2 participants were explicitly asked to make judgments about the presence or absence of BM in the stimulus. The early BM effect (100–200 ms) does not appear to be task-dependent in that it was observed with similar scalp topographies in both paradigms. Thus, these data point to a relatively involuntary process unrelated to explicit attention to the BM aspect of the stimuli. Of course, this effect could also reflect exogenous engagement of attentional-processes and since the color-detection task used in Experiment 1 could not be classified as an especially demanding task, it is entirely possible that subjects were able to devote some attentional resources to processing this aspect of the stimuli. However, the very early timing of this effect would argue against such an interpretation, and the large-scale differences in later cognitive components as a result of task make it clear that subjects did engage very differently in both tasks. Nonetheless, there is some experimental evidence for relatively automatic activation of BM processes. For example, Thornton and Vuong (2004) found that when task-irrelevant BM figures flanked a target BM figure, response times regarding the perceived direction of the centrally-presented figure were significantly prolonged, particularly when the flanking distractors' motion direction was incongruous with the target. That is, participants were
clearly unable to ignore the flanker BM stimuli. However, unlike the design used in Experiment 1 here, participants in the Thornton and Vuong study were explicitly attending for BM stimulus direction which complicates interpretation somewhat. Nonetheless, the task-independent early effects demonstrated here may represent the underlying neural processes behind such behavioral delays, as the brain involuntarily detects and processes irrelevant and potentially distracting BM signals.

**PHASE II EFFECTS (200–350 MS)**

The second major phase where BM processing effects were evident occurred between 200 and 350 ms and was characterized by a robust negative-going modulation of the ERP over the posterior middle temporal regions of both hemispheres. This negative deflection was evident in both Experiments 1 and 2, but it was also clearly amplified in Experiment 2 when the BM aspect of the stimuli was explicitly attended for. Differences between conditions in this middle phase of neuronal activity were in rough correspondence to the second component reported by Hirai et al. (2003) and what Jokisch et al. (2005) termed “N300”. Source analysis of this activity resulted in an excellent fit by a pair of equivalent current dipoles located bilaterally at or near the posterior STS. Given that these dipoles fall precisely between known activation locations within hMT and the pSTS, we think it very likely that they represent compound activity across an extended region comprising both of these regions (see Figure 7). Given the limited spatial resolution of scalp recordings, it was not possible to tease apart specific contributions from both regions using the point-dipole approach and one must be careful not to over-interpret the precision of such localizations. Rather, dipole locations are best thought of as centers-of-gravity for net local current flow rather than
discrete generator locations. These locations are highly consistent with pSTS effects previously reported in the neuroimaging literature (see Introduction section).

The pSTS has been implicated in many biological motion studies involving articulated human motion (Vaina et al., 2001, Beauchamp et al., 2002 and Grossman and Blake, 2002). However, neuroimaging studies have also shown that pSTS is engaged by considerably less complex motion stimuli, such as when the motion of simple two-dimensional objects depict social interactions (Heider and Simmel, 1944; Castelli et al., 2000; Schultz et al., 2003; and Ross and Olson, 2010). This is interesting since the two-dimensional motion of these geometric shapes is very different in terms of kinetic and perceptual properties to the point-light displays that were used here and in other biological motion experiments. Here, the points mark locations on human body parts that contort (e.g. arms and knees bending) when the body is in natural motion and that move in reference to one another evoking a vivid three dimensional impression. The fact that pSTS-regions are also activated in so-called “theory-of-mind” tasks, some of which employ static images or lexical tasks, suggests that pSTS-regions may be involved in processing of information that is more broadly related to social interactions (see Carrington and Bailey, 2009). Similarly, regions along the STS into the temporo-parietal junction are engaged in a variety of language related tasks (see Binder et al., 2009). Given the multitude of tasks for which pSTS involvement is indicated, Hein and Knight (2008) suggested that this brain region may support different functions depending on task-dependent network connections. In this view, pSTS activity is determined by coactivations of cell populations in other parts of a distributed neural network, and in the current work, it is likely the interaction with nearby hMT that
determines the pSTS role in processing BM.

Given the above evidence it seems plausible that networks within the STS are part of the semantic system supporting knowledge about the meaning of motion patterns and sequences. These structures can be engaged not only by dynamic BM stimuli, but virtually by any task involving or evoking meaningful motion such as static images or lexical or verbal descriptions of moving entities or agents. This could explain why this area is implicated in many tasks that are so different in nature, but also the consistency with which it is activated in experiments involving point-light displays that are often very similar in the types of activities they display.

BM and non-BM stimuli differ in basic and complex aspects of motion that can impact on early and late stages of the information processing stream. On a basic level, the dynamics of the point-lights in BM motion display a more patterned motion coherence and motion opponency (see Jastorff and Orban, 2009 and Casile and Giese, 2005) which leads to the emergence of a Gestalt on higher perceptual levels and will eventually engage neural networks involved in identification and conceptual knowledge encoded in higher order semantic networks. According to this notion, early lateral-occipital and occipito-parietal effects may be associated with differences in basic aspects of motion such as the spatiotemporal coherence of the motion of the point lights. Further, it is possible that there are automatic attentional mechanisms at play that are related to the binding of the point lights into a form similar to processes that precede the closure of fragmented objects in static displays (e.g. Snodgrass and Corwin, 1988). Indeed, the observed bilateral negativities observed during this second phase of BM processing bear strong resemblance to bilateral lateral-occipital negativities previously
described over both hemispheres during so-called perceptual closure tasks (e.g. using fragmented line drawings of common objects) that have been associated with the emergence of “objectness”, wherein associated fragments of a visual image are bound into a coherent and meaningful form (see e.g. Doniger et al., 2003, Sehatpour et al., 2006 and Sehatpour et al., 2008).

**Phase III Effects (400+ ms)**

The primary focus of this study was on sensory-perceptual stages of BM processing, but we also observed a robust later phase of processing that was BM-sensitive from approximately 400 ms onwards. This third phase of BM processing was only observed during Experiment 2 when the BM aspect of the stimuli was explicitly attended (see Figure 4 and Figure 5). This attention-driven effect was seen as a greater positivity in response to BM stimulation over midline central-parietal scalp. We speculate that this later sustained difference is associated with cognitive processes involved in decoding the meaning of the activity displayed by the motion stimulus. These higher order representations coding semantic features and associations, as well as their integration into abstract conceptual knowledge, are hypothesized to be widely distributed over the cortex according to an ‘embodied cognition’ view (Patterson et al., 2007). It seems likely that they involve parts of the premotor cortex which have been implicated in biological motion processing (Deen and McCarthy, 2010) and are considered to be part of a wider mirror neuron system (see Van Overwalle and Baetens, 2009). Such a widely-distributed network of activation is not easily modeled using the dipole source-modeling technique. Here, we found that a pair of bilateral parietal sources provided a good fit for this late effect but this solution likely represents a
significant over-simplification.

**CONCLUSION**

The detection and integration of biological motion (BM) information is a fundamental process of social cognition and involves a specialized cortical network. The present study used high-density electrical mapping and source-analysis techniques to provide a timeframe of information processing across this network. Scalp electrophysiology was recorded in response to canonical BM vs. scrambled motion (SM) stimuli in both a “BM-unattended” task and a forced-choice, attended-BM task. Our analyses resolved early effects beginning at ~100 ms with continuous significance achieved through 400 ms after stimulus onset, except for at the brief N1-peak time-window. The first phase of differential activation (110–170 ms) elicited a probable source in the dorsal stream superior to the KO/hMT complex. The second phase (200–350 ms) suggested bilateral sources between hMT and pSTS. An additional late (320 ms onward), occipital “positivity” occurred only when the distinction between BM and SM was explicitly attended. These results hopefully provide a framework for comparing the subtler information implicit in BM processing, such as familiar, complex motion processing, theory-of-mind processes, intentionality and perceived attention.

**ACKNOWLEDGMENTS**

This work was supported by grants to Professor Foxe from the U.S. National Institute of Mental Health (NIMH RO1 MH065350 and MH085322). A Graduate Science Fellowship from the City University of New York provided partial support for Mr. Krakowski during the initial stages of this project. Mr. Snyder received support from a Ruth L. Kirschstein National Research Service Award (NRSA) predoctoral fellowship.
from the NIMH (MH087077). We would also like to express our sincere gratitude to Dr. Manuel Gomez-Ramirez, Dr. Edmund Lalor, and the Cognitive Neurophysiology Lab team at the Nathan Kline Institute for all their help in this project. In addition, we wish to thank Dr. David Bloom, Dr. Randolph Blake, and their lab for providing us with the original stimuli.
CHAPTER II: TABLES AND FIGURES
Table 1: Summary of results of 3-way ANOVA with independent variables of task-type (attended vs. unattended), hemisphere, and motion-type (BM vs. SM). (* indicates significant results at $\alpha = 0.05$.)

<table>
<thead>
<tr>
<th>Component</th>
<th>ms</th>
<th>Task</th>
<th>Hem</th>
<th>Mot</th>
<th>Task X Hem</th>
<th>Task X Mot</th>
<th>Hem X Mot</th>
<th>Task X Hem X Mot</th>
</tr>
</thead>
<tbody>
<tr>
<td>eP1 P1</td>
<td>80–100</td>
<td>0.94</td>
<td>0.86</td>
<td>0.78</td>
<td>0.57</td>
<td>0.42</td>
<td>0.76</td>
<td>0.46</td>
</tr>
<tr>
<td></td>
<td>100–120</td>
<td>0.99</td>
<td>0.17</td>
<td>0.15</td>
<td>0.86</td>
<td>0.52</td>
<td>0.04*</td>
<td>0.34</td>
</tr>
<tr>
<td>P1–N1</td>
<td>120–170</td>
<td>0.65</td>
<td>0.91</td>
<td>0.01*</td>
<td>0.67</td>
<td>0.5</td>
<td>0.01*</td>
<td>0.79</td>
</tr>
<tr>
<td>N1 N1–P2</td>
<td>170–190</td>
<td>0.14</td>
<td>0.07</td>
<td>0.55</td>
<td>0.04*</td>
<td>0.28</td>
<td>0.07</td>
<td>0.60</td>
</tr>
<tr>
<td></td>
<td>190–240</td>
<td>0.03*</td>
<td>0.36</td>
<td>0.001*</td>
<td>0.01*</td>
<td>0.01*</td>
<td>0.77</td>
<td>0.88</td>
</tr>
<tr>
<td>P2</td>
<td>240–320</td>
<td>0.04*</td>
<td>0.19</td>
<td>0.001*</td>
<td>0.22</td>
<td>0.02*</td>
<td>0.23</td>
<td>0.25</td>
</tr>
<tr>
<td>N2</td>
<td>320–400</td>
<td>0.64</td>
<td>0.31</td>
<td>0.02*</td>
<td>0.44</td>
<td>0.39</td>
<td>0.02*</td>
<td>0.18</td>
</tr>
</tbody>
</table>
**Figure 1**: Sample stimuli: on the left are still-frames depicting normal biological activity in point-light animation sequences. On the right are the scrambled counterparts of the biological motion sequences.
Figure 2: Event-related componentry defined for the initial region-of-interest analysis.
Figure 3.(caption): VEPs for the unattended (a) and attended (b) biological motion (BM) tasks. Blue lines indicate the response to BM stimuli, red lines indicate the response to scrambled stimuli, and green lines represent the difference waves.
Figure 3:
**Figure 4 (caption):** Posterior topographic scalp maps of the response during both experimental conditions and the difference maps between them at selected time-points.
Figure 4:

100 ms  150 ms  200 ms  250 ms  300 ms  350 ms  400 ms  500 ms

BM

SM

diff

Unattended Task

BM

SM

diff

0.25 uV / step  Attended Task  reference free
Figure 5 (caption). Color-plot of t-values for the differences between canonical biological motion point-light displays and their scrambled counterparts in the unattended (a) and attended (b) tasks.
Figure 5:

A

- fronto-polar
- frontal
- fronto-central
- central
- parietal
- parieto-occipital
- occipital

B

- fronto-polar
- frontal
- fronto-central
- central
- parietal
- parieto-occipital
- occipital

Time (ms): 0, 100, 200, 300, 400
**Figure 6 (caption):** a. Scalp map of the difference between BM and SM responses at ~140 ms in the unattended task and the corresponding source localization for the 120-160 ms time-window (Talairach: x = 35, y = -69, z = -2; explained variance [EV] = 91%).
b. Scalp map of the difference between BM and SM responses at ~275 ms in the unattended task and the corresponding symmetric sources localized for the 200-350 ms time-window (Talairach: x = ±40, y = -69, z = 13; EV = 80%).
c. Scalp map at ~140 ms of difference-waves between scrambled and canonical biological motion for the attended task and the corresponding source localized for the 120-160 ms time-window (Talairach: x = 23, y = -80, z = 20; EV = 81%).
d. Scalp map at ~275 ms of the difference between scrambled and canonical biological motion for the attended task and the corresponding symmetric sources localized for the 200-350 ms time-window (Talairach: x = ±40, y = -65, z = 7; EV = 89%).
e. Scalp map at ~450 ms of the difference between scrambled and canonical biological motion for the attended task and the corresponding sources localized for the 400-500 ms time-window (Talairach: x = -37, y = -76, z = 16; x = 32, y = -77, z = 10; EV = 93%).
Figure 6:
CHAPTER III

SENSORY ROOTS OF SOCIAL DYSFUNCTION: BIOLOGICAL MOTION PROCESSING IN TYPICAL DEVELOPMENT AND THE AUTISM SPECTRUM
ABSTRACT

The visual processing of animate, biological motion (BM) is a fundamental neurocognitive function that is essential to normal social-cognition. In the present study, we used high-density EEG and point-light displays of upright (UM), inverted (IM) and scrambled BM (SM) to explore BM functioning in typical school-age children (TDs; N=46) and children with an autism spectrum disorder (cASD; N=35). In typical adults we previously identified three stages of neurophysiological processing over parieto-occipital scalp comprising an early, sensory-perceptual stage (100-200 ms) that was unaffected by explicit, task-relevant attention; a mid-level, motion-analysis stage (200-350 ms) that was susceptible to attentional influences; and a later, conceptual-analysis stage (400+ ms) that was only evoked when the presence of BM was task-relevant (Krakowski et al., 2011). In contrast, in the present study, school-age children showed distinctly immature neurophysiological responses to BM, with a single sustained phase of activity over parieto-occipital scalp that was statistically significant only from 250 ms onward and that was largely unaffected by attention. In cASD, basic visual processing (across all stimulus types) diverged significantly from the TD group, and analyses attuned to the clinical UM vs. SM effect revealed processing differences specific to BM processing. These data are considered within an ASD model of social dysfunction in which early perceptual deficits have cascading effects on higher-order processes.

Keywords: biological motion, electrophysiology, development, autism
INTRODUCTION

Social processing is a hallmark of human cognition and socially salient signals can be detected even from greatly impoverished sensory information. A prime example is the highly specialized ability to detect diverse social information, such as emotion, mood, and gender from biological motion (BM) point light displays (PLDs; see, e.g. Pollick et al., 2001; Kozlowski and Cutting, 1977). BM processing is of particular concern for those studying the typical development of social cognition, as well as developmental social cognitive dysfunctions, such as those seen in children with an autism spectrum disorder (cASD).

The behavioral literature to date demonstrates that sensitivity to upright BM PLDs is apparent as early as two days old (Simion, Regolin, and Bulf, 2008), with overall accuracy approaching adult levels by just five years of age (Pavlova et al., 2001, Blake et al., 2003), though response times (RTs), as well as subtler BM-related processes, likely differ substantially. In school-age children (7-14 years) and adults, Hirai et al. (2009) reported an earlier electrophysiological P1-component as well as amplified N1 and N2 over occipitotemporal sites in response to BM vs. scrambled motion (SM), in many respects similar to the effects we have shown in adults (Krakowski et al., 2011).

There is substantial controversy in the recent behavioral literature as to whether BM-processing deficits are implicated in the autism spectrum disorders (ASD; see Table 2). The earliest findings regarding the potential role of a BM-specific deficit in ASD were negative. Namely, Moore, Hobson, and Lee (1997) reported a significant impairment in autistic children and adolescents in the inference of internal emotional and mental
states from BM PLDs, but not in the categorization of overt BM actions (e.g. running, jumping, etc.), suggesting that the dysfunction was not directly related to BM-processing. Similarly, Hubert et al. (2007) found only a significant impairment in detecting implicit emotions from BM PLDs in high-functioning young adults with ASD (21±6 years). Parron et al. (2008) also found no effect for BM processing per se, instead reporting deficits specific to the detection of emotion from BM PLDs in subjects with ASD (age = 11±3 years), a pattern of findings more consistent with an emotion-processing dysfunction rather than a general BM-processing disorder. Saygin, Cooke, and Blakemore (2010) reported comparable psychophysical thresholds for BM detection in noise in adults with ASD, and most recently, Rutherford and Troje (2011) found no difference between autistic adults and typical controls in the perception of BM, instead reporting a significant correlation between BM perception and IQ in the participants with ASD.

In contrast to these findings pointing to a lack of BM-specific dysfunction, Blake et al. (2003) reported that sensitivity scores (d-prime) in a simple BM-categorization task were significantly lower in cASD than in mental-age matched typically developing controls (TDs), and were also correlated with the severity of the disorder. Annaz et al. (2010) reported that for children of 5-12 years, while TDs steadily improve in perceptual sensitivity to BM (also as measured by d-prime sensitivity scores), children with ASD showed a flat developmental trajectory, overlapping with TDs only at the youngest age. Koldewyn, Whitney, and Rivera (2010) also reported higher thresholds for detecting BM in noise amongst adolescents with ASD. Similarly, Atkinson (2009) found a BM processing deficit in adults with ASD, as well as a significant correlation between
emotion detection and motion coherence processing. Kaiser et al. (2010b) suggest that while those with ASD are able to process BM, they lack the typical enhancement of visual sensitivity to BM relative to object motion. One possibility is that this dysfunction results from early attentional differences in very young children with ASD who do not appear to preferentially attend to BM (see Klin and Jones, 2008; Klin et al. 2009; Annaz et al. 2011).

While the behavioral research to date has been at best inconsistent, without any clear explanation for the divergent findings, recent neuroimaging studies do seem to point to atypical processing of BM in those with ASD. Herrington et al. (2007) reported that while both participants with Asperger’s syndrome (ASp) and typical adults reached ceiling levels on direction discrimination of BM PLDs, the ASp group showed less activity in superior temporal areas during these tasks. Freitag et al. (2008) reported that adolescents and adults with ASD had longer response times in categorizing coherent BM and scrambled motion (SM), as well as significantly reduced activity in parietal and temporal areas. Koldewyn, Whitney, and Rivera (2011) found that adolescents with ASD had reduced activity in the posterior superior temporal sulci (pSTS), parietal, and frontal cortices relative to controls in a BM-in-noise direction discrimination task, with dorsolateral prefrontal activity negatively correlated with symptom severity. More recently, McKay et al. (2011) conducted an fMRI study of adults with ASD and typical controls matched for age and IQ. Behaviorally, participants with ASD demonstrated normal thresholds for detecting the direction of partially scrambled point-light walkers. However, their fMRI activation patterns were atypical and a follow-up connectivity analysis suggested the use of two isolated form and motion networks in place of the
integrated temporal-to-parietal activation seen in the TD controls (see McKay et al., 2011). Finally, Kroger et al. (2013), in the only electrophysiology study of BM in ASD to date that we are aware of, found significant differences between the early VEPs of cASD and TDs for both BM and SM. However, there was no interaction between motion-type and group for the sites tested, which would have indicated a specific BM impairment in ASD. All-in-all, the common thread that does still appear to emerge from these studies is a fairly consistent hypoactivation of the BM response in pSTS and/or adjacent areas in those with ASD relative to their TD peers (see Table 2).

While the small number of imaging studies do indeed point to a specific BM processing dysfunction, the low temporal resolution of these methodologies leaves open the question of whether atypical BM processing is already seen at early, perceptual stages of neural processing, or only reflects later cognitive differences. The fact that performance of BM-related tasks during many of these studies appeared to be typical surely further complicates interpretation of the findings. Until more is known both about the typical development of the different spatiotemporal stages of BM processing, as well as at which levels BM-processing is affected in ASD, it is impossible to form a clear picture of the meaning BM has within the larger domain of social cognition. The implications of such a knowledge-base are potentially profound, both in enabling a more fundamental understanding of typical social cognition, as well as in providing new frameworks for treating social-cognitive dysfunctions at their roots. As such, there is a strong need for more neurophysiological research that can focus on the component spatiotemporal events that comprise neural BM-processing. While the only study on the electrophysiology of BM in ASD (Kroger et al, 2013; see above), did report significant
effects of group (ASD vs. TDs) over occipito-temporal sites (O1, O2, P9, P10), their findings were equivalent for both BM and SM. Without any significant interaction between motion-type, it remains inconclusive at best if a specific BM impairment is at all involved in the dysfunctions of ASD. However, considering their relatively modest group size (ASD: N=17; ages 6-15 years), as well as the fact that the sites analyzed did not include those we previously found to be optimal for detecting BM processing in adults (PO7, PO8; see Krakowski et al., 2011), the question of a role for early BM-processing dysfunctions in ASD remains unclear. In addition, the role of attention in BM-processing has yet to be explored in either TD or ASD populations. Considering the clear role of attention in the BM VEP in typical adults (see Krakowski et al., 2011), this information is particularly salient in informing both our conception of normal social-cognitive development, as well as of its dysfunctions.

Using electrophysiology in typical adults, we have mapped out a three-stage trajectory of BM processing, consisting of: 1) an early sensory-perceptual phase localized to dorsal stream motion-processing regions, 2) a mid-level motion analysis phase localized to the posterior superior temporal gyrus that is susceptible to attentional influences, and 3) a later conceptual analysis phase only when BM is task-relevant (Krakowski et al., 2011). The present study will use a similar approach to map the developmental trajectory of the neural processes underlying BM processing in a large cohort of school-aged children and adolescents (N=46). In addition, these data will serve as a benchmark against which we will compare the spatiotemporal neurodynamics of biological motion processing in children with ASD (N=35). By exploring the VEPs of TDs and cASD in response to both unattended BM and task-
relevant, attended BM, the exact role of an essentially sensory-perceptual process in higher-order social cognition can be more clearly determined, inasmuch as earlier effects and areas can plausibly be said to feed later ones.

**METHODS**

**PARTICIPANTS**

Thirty-five children with ASD (cASD; aged 6-16 yrs.), along with 46 age-matched typically developing children (TDs) participated in these experiments (see Table 3). Participants were screened for normal or corrected-to-normal vision in both eyes. Parents of participants on stimulant medication were asked to refrain from administering the stimulant medication during the 24-hour period prior to electrophysiological testing. A diagnosis of autism was confirmed through the Autism Diagnostic Interview-Revised (ADI-R; Lord, Rutter, & Le Couteur, 1994), the Autism Diagnostic Observational Scale (ADOS; Lord *et al.*, 2000), as well as through licensed clinical judgment. Age-appropriate abilities in cognition, language, and academic skills were confirmed in the TDs by normal range scores on a battery of standardized tests of cognition, language, and adaptive functioning. All children were administered the following battery of standardized tests for the purposes of characterizing and matching the samples: The Wechsler Abbreviated Scales of Intelligence (1999); The Harris Tests of Lateral Dominance (Harris, 1974); The Vineland Adaptive Behavior Scales – Second edition (Vineland-II; Sparrow, Ballee, & Cicchetti, 1984); the Clinical Evaluation of Language Fundamentals - Fourth edition (CELF-4; Semel, Wiig, & Secord, 2003) and the Peabody Picture Vocabulary Test – III (Dunn, 1997).
The parent or guardian of each child provided written, informed consent. All procedures had prior approval by the institutional review boards of the Albert Einstein College of Medicine and the City University of New York, and were in accordance with the Declaration of Helsinki. Participants received modest remuneration for their time.

**STIMULI AND TASKS**

Displays were presented on a 26" ViewSonic® VP2655wb monitor controlled by Neurobehavioral Systems™ Presentation® software. All experiments were conducted in a sound-attenuated electrically shielded room illuminated by light from the video screen. All stimuli appeared as black against a white background. Participants were instructed to maintain fixation on a central fixation-cross and eye-position was monitored by vertical and horizontal electrooculogram. Video-clips of an adult human engaged in common activities (e.g. running, kicking, climbing, throwing, and jumping) were imported to a computer to create the biological motion stimuli. Markers were placed on the actor’s joints in each frame of the sequence, such that the final clips were only composed of up to twelve moving dots (i.e. point-light displays). Scrambled motion (SM) sequences were created from the normal biological animations and consisted of the same individual dots undergoing the same local motions as the biological counterparts. Scrambling was achieved by randomizing the spatial locations of the dots in a given animation, thereby distorting the hierarchical, pendular motions that are characteristic of biological motion. As such, SM only retains intact local motion information that is insufficient for the perception of a human actor, thus establishing a control stimulus for undistorted, upright BM (UM). Inverted biological motion (IM) sequences were created from the normal, upright sequences (UM) by rotating the
images 180 degrees (see figure 1a). IM retains the overall global configuration of the PLDs and is generally detectable as BM at least in adults. Nonetheless, IM are not as readily interpretable as UM (see Simion, Regolin, and Bulf, 2008; Grossman and Blake, 2001; see also Chang and Troje, 2009). The methodology behind the generation of biological motion sequences is discussed more fully in Grossman and Blake (1999) and Blake et al. (2003).

The experiments consisted of two two-alternative-forced-choice tasks in each of which participants were presented with six five-minute blocks of randomly ordered video-clips of all three stimulus types (UM, SM, and IM). The “unattended” task targeted the automatic processing of BM while the participants performed a distractor task. To this end, in all clips, one of the dots briefly (4 frames) turned either red or green. In the “unattended” task, participants were instructed to respond to the color-change by depressing one of two mouse keys. To ensure that attention was maintained throughout the duration of the clip to the entirety of the display, without reliance on prior experience, this color change occurred at both random time and location. To maintain presumed naïveté in the unattended task, participants were not explicitly informed that some of the clips portrayed human motion until the “attended” task which always followed completion of the entire unattended task. As such, the electrophysiological differences in response to the different stimuli could be said to reflect an involuntary, automatic processing of BM.

In the second, “attended” task, participants were once again presented with the same video clips. This time, however, participants were asked to judge whether or not the clips depicted human motion (“the dots move like a person” [both upright and
“upside-down”] vs. they “don’t look like a person”). As such, the second task explored the voluntary and intentional processing of BM. The same stimuli, including the color-changing dot, were used in both tasks to ensure that differences found in the responses to the two tasks were clearly reflective only of the actual task difference.

In total, 120 distinct video-clips were used, forty of which represented upright point-light displays of canonical biological motion (see below), forty of which represented inverted point-light displays of canonical biological motion, and forty of which represented scrambled biological motion. Each clip was composed of 29 frames presented at the monitor refresh-rate of 60 Hz, for a total frame-duration of 17 ms and a total clip-duration of 483 ms. Because the practical constraints involved in studying young and/or clinical populations necessitated relatively brief recording sessions, the inter-stimulus interval was also kept relatively short (500-1000 ms) to ensure that sufficient electrophysiological data could be obtained for analysis.

Both tasks were preceded by a set of practice trials to ensure participants understood the task. Over the course of both tasks, participants were encouraged to take breaks between blocks as necessary, in order to maintain high concentration and reduce fatigue.

**MEASUREMENTS AND ANALYSES**

**BEHAVIORAL ANALYSES**

D-prime scores were calculated for the three stimulus types (UM, IM, SM) and the groups (cASD, TDs) were compared using a general linear model with covariates of sex, IQ, and age. In signal detection theory, D-prime serves as an index of the actual
signal relative to the noise and can be measured as the difference between the normalized hit rates and false alarm rates (see Green and Swets, 1966). In addition, miss rates were also computed and analyzed using a generalized linear model, once again with covariates of sex, age, and IQ. For all analyses, alpha criterion was set at $\alpha = 0.05$.

**ELECTROPHYSIOLOGY**

Continuous EEG was acquired through the ActiveTwo BioSemi™ electrode system from 72 scalp electrodes, digitized at 512 Hz (see figures 2-4). Data were filtered with a low-pass 0-phase shift 40 Hz 96 dB filter after acquisition. BioSemi™ replaces the ground electrodes used in conventional systems with two separate electrodes: Common Mode Sense (CMS) active electrode and Driven Right Leg (DRL) passive electrode. These two electrodes form a feedback loop, rendering them references. For a detailed description of the referencing and grounding conventions used by the BioSemi™ active electrode system, visit www.biosemi.com/faq/cms&drl.htm.

Data were analyzed and artifacts rejected offline using the BESA™ multimodal neuroimaging analysis software package (MEGIS Software GmbH, Munich, Germany). Accepted trials were epoched (100 ms prestimulus to 500 ms post-stimulus) and then averaged separately for each condition. Baseline was defined as the mean voltage over 100 ms preceding the onset of the stimulus. Trials with blinks and large eye movements were rejected offline on the basis of horizontal and vertical electrooculogram recordings. An artifact rejection criterion of $\pm 140 \mu V$ was used at all
other electrode sites to exclude periods of high EMG and other noise transients. Averages were computed for each subject from the remaining artifact-free trials. A Kolmogorov-Smirnov test was used to ensure SNRs corresponded between the groups.

**EEG ANALYSIS STRATEGY**

Because there was little-to-no literature regarding the precise timing of the electrophysiological response to BM stimuli in typically developing children and children with ASD and because of the complexity of our data set, a two-stage approach to the statistical analyses was implemented. The initial analysis implemented a generalized linear model of the VEPs for all main effects (task, motion-type, clinical group, hemisphere) as well as interactions using time-windows defined by maximal activity (peaks) over two bilaterally-symmetric channels over parieto-occipital scalp (PO7 and PO8) as guided by our work in typical adults (Krakowski et al., 2011). The subsequent analysis focused on the main question of differences in processing BM in ASD by implementing a more powerful hierarchical linear modeling paradigm in order to more thoroughly investigate the primary effect of interest, i.e. the group BM effect as measured by the UM-SM difference, over expanded regions-of-interest (ROIs) that encompassed six pairs of bilateral parieto-occipital sites, and used contiguous time-windows from 100 ms onward. What follows is a brief description of these two analyses.

**Stage one analysis: General motion-type effects and interactions**

In order to explore the full set of the main effects of BM-processing and attention in typical development and in ASD as well as their interactions, while limiting type-II
errors, the initial analysis was restricted both spatially and temporally. Accordingly, based on the findings in the previous literature on the developing VEP in response to BM (Hirai et al., 2009), as well as findings in typical adults using a similar paradigm (Krakowski et al., 2011), a pair of bilateral regions-of-interest were defined comprising electrode sites on or near the temporo-parieto-occipital junctions bilaterally (PO7 and PO8), from where we have previously recorded BM-related activity that was sourced to underlying higher order visual-processing areas such as pSTS. Areas-under-the-curve were computed for VEP components that were defined based on grand-averaged waveforms collapsed across all groups, tasks, and stimuli (i.e. without regard for or bias from the dependent measures of interest). These ultimately encompassed five time-windows centered at peak activity (P1 = 129-159 ms; N1 = 200-230 ms; P2 = 250-300 ms; N2 = 300-350 ms; and P3 = 350-500 ms; see figures 1b and 5). As the earliest components were more “dynamic” i.e. had higher frequencies, their duration is correspondingly shorter than the later, lower frequency components. The alpha criterion was set at 0.05. Data were analyzed using a generalized linear mixed model design with a between-subjects factor of group (cASD, TDs) and within-subject factors of motion-type (UM, SM, IM), task (unattended, attended), and hemisphere (right, left), as well as covariates of sex, age, and IQ.

Stage two analysis: hierarchical linear model of motion-type difference waves X clinical group interactions

Our initial analysis dealt with a large number of factors and was therefore statistically quite conservative with a correspondingly increased likelihood of Type-II errors. In view of this, we also implemented a more powerful random-regression
hierarchical linear modeling (HLM; Bryk et al., 1992; Gibbons et al., 1998) approach for the primary focus of BM-processing effects in ASD, using the between-group effects for the UM-SM difference waves, for both tasks (unattended and attended). In contrast to traditional ANCOVA analyses, HLM allows for heterogeneity among groups and takes into account the time-dependent correlation structure of the observations (sampling points). In the HLM model, repeated assessments of the difference wave within each specified time window served as the dependent variable. The two independent variables were “clinical group” (cASD, TDs) and “time” (sampling point relative to stimulus onset). Least-square means (LSMs) effects were tested to determine a significant effect within a group. To limit the number of comparisons and resultant type-II errors, as well as computational cost, only the group effects (cASD, TDs) on the difference between UM and SM for the specified time-windows were analyzed.

Group (cASD, TDs) served as the between-subject factor, and time (ms) as the within-subject, random effect factor. Fixed-effect covariates were once again: sex, IQ, and age. To further increase the power of our analysis, ROIs included the bilateral sites of our initial GLM analysis (PO7 and PO8), as well as eight adjacent sites (O1, O2, PO3, PO4, P5, P6, P7, and P8), for a total of ten bilaterally-symmetric sites. The temporal range of data was also expanded to fully encompass the post-stimulus sequence from 100 ms onward, with new time-windows of a minimum of 50 ms (P1a = 100-150 ms; P1b = 150-200 ms; N1' = 200-250 ms; P2 = 250-300 ms; N2 = 300-350 ms; and P3 = 350-500 ms). The Hochberg method (Hochberg, 1988) was employed to correct for multiple comparisons using an alpha criterion of .05. To additionally reduce the likelihood of Type-I errors, an effect was only considered if
significance was reached at a minimum of two adjacent sites. (See also De Sanctis et al. [2012] for a similar approach.)

RESULTS

BEHAVIORAL FINDINGS

Though on average cASD did appear to perform slightly more poorly than TDs (see table 4), these group differences did not reach or even approach significance for any of the three stimulus types, neither for d-prime scores nor for miss rates (see table 5). Effects of age and IQ were significant for d-prime scores, but not for miss rates. There were no significant effects of sex (see table 5).

ELECTROPHYSIOLOGY

STAGE ONE ANALYSIS: GLM OF MAIN EFFECTS AND INTERACTIONS

In the initial analysis, data were analyzed using a generalized linear mixed model design with a between-subjects factor of group (cASD, TDs) and within-subject factors of motion-type (UM, SM, IM), task (unattended, attended), and hemisphere (right, left), as well as covariates of sex, age, and IQ.

P1

For the P1 component (129-159 ms), there were main effects of group ($F = 9.96, p = 0.0023; df = 1,76$), age ($F = 19.66, p<0.0001; df = 1,76$), sex ($F = 77.83, p<0.0001; df = 1,76$), and IQ ($F = 98.13, p<0.0001; df = 1,76$). There were no significant interactions between any of the factors. Group effects were due to more positive amplitudes for cASD (see table 6 and figures 2-5).
For the N1 component (200-230 ms), there were main effects of group (F = 393.09, p<0.0001), task (F = 4.12, p = 0.0456), age (F = 268.13, p<0.0001), sex (F = 430, p<0.0001), and IQ (F = 93.98, p<0.0001). Once again, there were no significant interactions. Group effects were due to less negative N1 amplitudes for cASD. Task effects were due to amplified negativity for the attended task (see table 6 and figures 2-5).

For the P2 component (250-300 ms), there were main effects of group (F = 48.31, p<0.0001), motion-type (F = 5.75, p = 0.0039; df = 2,158), age (F = 84.23, p<0.0001), sex (F = 182.92, p<0.0001), and IQ (F = 5.76, p = 0.0189), as well as a trend toward significance for task (F = 3.63, p = 0.0603; df = 1,79). There were no significant interactions. Group effects were due to more positive amplitudes for cASD. Post-hoc tests of the motion-type effect (UM, IM, SM) revealed that the responses to UM and IM were not significantly different from each other (t = -1.16; p = 0.2492), but were both of significantly more negative amplitude than the response to SM (UM vs. SM: t = -3.34; p = 0.0010; IM vs. SM: t = -2.18; p = 0.0305; see table 6 and figures 2-5).

For the N2 time-window (300-350 ms), there were main effects of group (F = 19.80, p<0.0001), motion-type (F = 8.00, p = 0.0005), sex (F = 153.15, p<0.0001), and IQ (F = 4.87, p = 0.0303). Again there were no significant interactions for any of the factors. Group effects were due to less negative amplitudes for cASD. Post-hoc tests revealed that the response to SM was of significantly less negative amplitude than that of UM (t = -4.00; p < .0001) or IM (t = -2.17; p = 0.0316), and IM trended toward a less
negative amplitude than UM ($t = -1.83; p = 0.0696$; see table 6 and figures 2-5).

**P3**

Finally, for the P3 component (350-500 ms), there were main effects of group ($F = 29.78, p<0.0001$), motion-type ($F = 5.17, p = 0.0067$), age ($F = 106.17, p<0.0001$), and sex ($F = 68.19, p<0.0001$). There was also a significant interaction between group and hemisphere ($F = 6.45, p = 0.013$; df = 1,79), with significantly greater amplitudes over the left hemisphere relative to the right only in cASD ($t = 2.50; p = 0.0145$; see figure 4). As with the other four windows of analysis, group effects were due to more positive amplitudes for cASD. Post-hoc tests of the motion-type effect revealed that the response to UM was of significantly less positive amplitude than that of SM ($t = -3.20; p = 0.0017$). The response to IM trended toward less positivity than SM ($t = -1.91; p = 0.0580$; see table 6 and figures 2-5).

In summary, there were group effects (cASD, TDs) in the VEP to BM PLDs for every time-window tested. In addition, there were motion-type effects (UM, IM, SM), regardless of group, from 250 ms onward. There were, however, no significant interactions between group and motion-type. This conventional analysis, which was similar to the methodology used in investigating the spatiotemporal dynamics of BM-processing in adults, was followed by a more statistically-sensitive approach directed specifically at the question of group differences with regard to the BM effect as measured by the difference between UM and SM.

**Stage Two Analysis: Hierarchical Linear Model of the Group Biological Motion Effect**

The secondary analyses of clinical group effects focused specifically on the BM
effects as indexed by the differences between the electrophysiological responses to UM and SM. These analyses found that, in the unattended task, there were indeed significant effects of clinical group (cASD vs. TDs) for the UM-SM contrast during N1' (200-250 ms) over P6, P8, and PO8, as well as during P2 (250-300 ms) over P8 and PO8. In the attend-motion-type task, there were significant group effects during N1' over PO8 and P6 and during P2 over P5 and P7 (see table 7). All significant effects were in the direction of larger differences between UM and SM in TDs than in cASD for all sites and tasks that met criteria (see table 7 and figures 6 and 7). All other effects in this analysis did not meet criteria for significance.

**DISCUSSION**

When processing biological motion stimuli (BM), children with ASD (cASD) showed behavioral responses, as well as scalp-recorded neurophysiological activity that were substantially similar to those of typically developing controls (TDs). Both groups demonstrated clear segregations between their responses to upright biological motion (UM) and scrambled motion (SM) from 250 ms onward, with the overall amplitude of the response to inverted motion (IM) intermediate between the amplitudes of the other two stimulus-responses (UM, SM). However, more powerful secondary analyses focused specifically on a potential neurophysiological BM dysfunction in ASD indeed indicated that there were EEG differences between the two groups specific to BM-processing.

**TYPICAL ELECTROPHYSIOLOGY OF BIOLOGICAL MOTION PROCESSES**

As mentioned in the introduction, a previous study of typical adult BM processes revealed three waves of activity over bilateral parieto-occipital sites. While the earliest
phase of activity (100-200 ms) was unaffected by attention task, the second phase
(200-350ms) was amplified by attention, and the third phase was only evident in the
attended task (see Krakowski et al., 2011). In contrast, school-age children appear to
show only one extended wave of neurophysiological activation in response to BM
stimuli that onsets considerably later than is seen in adults, beginning from 250 ms
onward. Nonetheless, motion-type effects remained task-invariant and there was no
significant interaction between motion-type and task (see table 6). While previous
behavioral studies have shown that some BM processing would appear to be innate and
present from birth (see e.g. Simion, Regolin, and Bulf, 2008), it is clear from the present
findings that the visual system continues to tune its processing of these fundamental
stimuli since the early processing stages as well as attentional effects seen in adults
have yet to mature.

Previously, Hirai et al (2009) found amplifications of the amplitudes of the
negative peaks in the 100-280 ms (“N1”) and 220-500 ms (“N2”) time-windows in
response to a laterally viewed PLD of a walking person (PLW) relative to its scrambled
counterpart, in school-age children. Overall, our findings are consistent with their “N2”
effect. It remains unclear if the “N1” amplification in that study was the result of
divergent analytical techniques, or a genuinely earlier physiological response to the
more predictable dynamics of the PLW. Notably, even their “N1” time-window extends
past 250 ms where we also found significant effects. Also, most recently, in their study
of the developing BM VEP, Kroger et al. (2013) did not report any such motion-type
effect, though this was possibly due to insufficient power. Regardless, the positive
findings of the secondary analysis of ASD BM effects in the present study from 200 ms
are consistent with earlier BM processes, which may also be implicated in the Hirai et al. (2009) study.

Furthermore, from the VEPs in the present study, it is quite clear that this BM-processing phenomenon is not solely an amplification of VEP peaks, but rather a long negative deflection in response to intact BM. In fact, this long BM-negativity closely resembles object closure neurophysiology seen in static image processing. For example, a relatively large negativity over bilateral occipito–temporal sites occurs in the 230–400 ms time-window in response to coherent, fragmented, static images relative to their spatially-scrambled counterparts in adults (see e.g. Doniger et al., 2000; Sehatpour et al., 2006).

The resultant, meaningful cognitive constructs obtained in object closure may share similarities with BM. However, the basic sensory processes implemented in at least the initial phases of object construction from static image information are arguably functionally and anatomically distinct from those that rely on spatially-sparse, dynamic information of point-light displays. Thus, for example, while static object-closure processes implicate ventral-stream form processing areas such as the lateral occipital complex (LOC), BM-processing relies more heavily on dorsal-stream motion areas and has been shown to be distinctly processed by pSTS (see chapter I).

In light of the dynamic nature of the human brain in general, that these processes continue to develop through childhood and adolescence is hardly surprising. And while static image processing in the autism spectrum may appear to be relatively intact (see Spencer et al., 2000; Blake et al., 2003; Del Viva et al., 2006; Bolte et al., 2007; de
Biological motion in ASD

Jong et al., 2007; Kemner et al., 2007; Milne et al., 2006; see also, however, Bertone et al., 2003; 2005; Brosnan et al., 2004; Tsermentseli et al., 2008; Brandwein et al., 2011 and Frey et al., 2013), BM-closure processes remain a ripe candidate for an underlying sensory-perceptual etiological root to social-cognitive deficits in ASD. This is particularly the case when one considers perspectives such as the “dorsal stream vulnerability” model of ASD, i.e. that visual processing typically dependent on dorsal-stream areas is specifically affected in ASD and other developmental disorders (see, e.g., Pellicano et al., 2005).

**Biological motion processing in the Autism Spectrum**

In the present study, an initial analysis of two bilateral parieto-occipital sites previously shown to be particularly implicated in BM EEGs (PO7, PO8; see Krakowski et al., 2011) showed substantial between-group (cASD vs. TDs) visual processing differences, without distinction between the three stimulus classes (UM, IM, SM; see also Kröger et al., 2013). This finding could perhaps be interpreted as indicative of general, complex visuo-motion processing dysfunctions in ASD. The literature to date has been at best inconsistent regarding complex motion processing deficits in ASD (see e.g. Bertone et al., 2003; Davis et al., 2006; de Jonge et al., 2007; Del Viva et al., 2006; Milne et al., 2002; Milne et al., 2006; Pellicano et al., 2005; Spencer et al., 2000; for a thorough review, see Kaiser and Shiffrar, 2009), so this finding of a pronounced visual processing dysfunction for three classes of BM stimuli is quite significant.

Furthermore, considering that all three stimulus types reflect aspects of social information (e.g. minimum jerk; see Cook et al, 2009), albeit in altered forms, these findings are also perhaps suggestive of a role of complex visual processing impairments
in the etiology of the social dysfunctions associated with the disorders. It is important to note that because our focus was on distinguishing coherent and incoherent BM processes, the possibility remains open that these across-the-board effects are really the result of basic visual processing differences (see e.g. Brandwein et al. 2013; Frey et al., 2013).

Because our initial analysis had a large number of factors and therefore a heightened risk of type-I errors, a more-powerful secondary analysis tuned to BM-specific differences in ASD was also implemented. Indeed, from 200 to 250 ms (N1’), this second analysis showed significant UM-SM group differences over the right hemisphere for both tasks (see figure 6). There were also significant between-group effects from 250 to 300 ms (P2) over the right hemisphere for the unattended task and over the left hemisphere for the attended task (see table 7 and figure 7). Overall, these results support the neuroimaging literature that reports a specific BM-dysfunction in ASD particularly in occipitotemporal regions such as pSTS (see, e.g. Freitag et al., 2005; Herrington et al., 2007; Kaiser et al., 2010b; see Introduction).

Both effects (N1’ and P2) appeared to be due to an amplified negative deflection in response to UM relative to SM in typical development from 200 to 300 ms which, while present, was dampened somewhat in ASD (see figures 2 and 3). Interestingly, while this between-groups effect was exclusively right-lateralized for N1’ without regard to attentional task, for P2, it was right-lateralized only in the unattended task, and was left-lateralized when participants were explicitly instructed to attend the presence of BM. While BM is typically processed by both hemispheres, a common finding in the literature is an amplified response to BM stimuli in the right hemisphere relative to the left (see
e.g. Peuskens et al., 2005; see also, however, Krakowski et al., 2011). Plausibly, right-lateralized between-group effects seen in both tasks of our study reflect a basic, involuntary, sensory-perceptual BM-processing dysfunction in cASD, while left-lateralized P2 effects represent higher-order cognitive-attentional deficits. In accordance with this, Kaiser et al. (2010b) reported a negative correlation between social responsiveness scores, in which cASD are impaired relative to TDs, and pSTS activity specifically in the right hemisphere, in a passive BM-viewing task that didn’t depend on higher-order cognitive processes.

Similarly, these findings also perhaps correspond with those of Herrington et al. (2007) who reported significantly decreased BOLD responses in adults with Asperger’s syndrome (AS) in response to point-light walkers. In their findings, between-group effects were more posterior in the right hemisphere than in the left, which in light of our findings, perhaps indicate an earlier latency for the dysfunction in right brain regions than in left. While their direction-discrimination task explicitly incorporated intentional BM-processing, their right-lateralized network of hypoactivation spanning cerebellar, fusiform, temporal, and occipital areas would plausibly be implicated in automatic, unintentional BM-processing as well. While they did not find any areas of significant interaction between clinical group and motion-type, this was likely due to the fact that their unique SM stimuli still retained much of the configural information of intact BM, as well as due to acknowledged insufficient power. This seems particularly plausible considering that their SM stimuli elicited a dramatically different between-group hypoactivation map than that of their intact BM stimuli, with only one cluster of hypoactivation in AS in the right, inferior parietal lobe. Notably, our initial analysis also
failed to discover significant interactions between motion-type and group, which were only teased out by the more focused secondary analysis.

Overall, the task-invariant difference between UM and SM that was significantly attenuated in cASD is consistent with findings that cASD are not as susceptible to the automatic capture of attention by socially salient stimuli (see, e.g., Klin et al., 2009; see also Jellema et al., 2009). Even when participants were focused on a distractor task and not cued to the presence of BM, TDs had amplified neural responses distinguishing UM and SM, likely suggesting an automatic and involuntary allocation of attentional resources to BM processing. While cASD also had a similar visual evoked response segregating stimulus-types even in the unattended task, the effect was significantly dampened, indicating that the dysfunction is not limited to scenarios where BM is explicitly cued as task-relevant. In addition, the earliness of the effects suggests that BM processing differences are not limited to attentional and social-cognitive dysfunctions. Similarly, our initial findings of robust between-group effects without regard to stimulus-type are a strong indication of a basic sensory-perceptual deficit in ASD with direct relevance to social cognition. As such, it appears fairly clear that ASD are associated with early, perceptual disorders with regard to relatively low-level social-visual processing. This finding supports a model of ASD whereby specific visual deficits early in development may feed the social-cognitive dysfunctions that are a hallmark of the disorders.

CONCLUSION

School-age children showed immature VEPs in response to biological motion
Biological motion in ASD

84

stimuli (BM) with only one wave of activation that was unaffected by attentional task and that began only from 250 ms onward, over parieto-occipital sites. Children with ASD demonstrated essentially typical ability at BM detection, as well as a similar gross electrophysiological signature in response to BM stimuli, without regard to attentional task. Large group differences did emerge, but for all three stimulus types (upright BM, inverted BM, scrambled BM), suggesting substantial clinical differences in general visual processing, perhaps due to the complex motion content. In addition, a secondary analysis suggested that subtle processing anomalies in BM processing in ASD do indeed exist, from 200 to 300 ms, lending credence to a model of ASD where social dysfunctions may be fed by early perceptual deficits.

ACKNOWLEDGMENTS

Primary funding for this work was provided through a grant from the U.S. National Institute of Mental Health (MH085322 to J.J.F. & S.M.). The Human Clinical Phenotyping Core, where the children enrolled in this study were clinically evaluated, is a facility of the Rose F. Kennedy Intellectual and Developmental Disabilities Research Center (IDDRC) which is funded through a center grant from the Eunice Kennedy Shriver National Institute of Child Health & Human Development (NICHD P30 HD071593).

We would like to thank Drs. Julianna Bates, PhD, Alice Brandwein, PhD, John Butler, PhD, Menahem I. Krakowski, MD, PhD, Natalie Russo, PhD, Pejman Sehatpour, MD, PhD, and Adam C. Snyder, PhD for their invaluable assistance and advice. We also extend appreciation to Frantzy Acluche, Christine Alaimo-Collins, Edel Flynn,
Sarah Ruberman, and the rest of the staff at the Tishman Cognitive Neurophysiology Laboratory for their involvement in this project.
CHAPTER III: TABLES AND FIGURES
### Table 1: Abbreviations used in this chapter.

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASD</td>
<td>autism spectrum disorder</td>
</tr>
<tr>
<td>BA</td>
<td>Brodmann’s area</td>
</tr>
<tr>
<td>BM</td>
<td>biological motion</td>
</tr>
<tr>
<td>BMW</td>
<td>biological motion display of walking human</td>
</tr>
<tr>
<td>cASD</td>
<td>children with autism spectrum disorders</td>
</tr>
<tr>
<td>CM</td>
<td>coherent biological motion</td>
</tr>
<tr>
<td>EEG</td>
<td>electroencephalography</td>
</tr>
<tr>
<td>ERP</td>
<td>event-related potential</td>
</tr>
<tr>
<td>fMRI</td>
<td>functional magnetic resonance imaging</td>
</tr>
<tr>
<td>GLM</td>
<td>generalized linear model</td>
</tr>
<tr>
<td>GoF</td>
<td>goodness-of-fit</td>
</tr>
<tr>
<td>HLM</td>
<td>hierarchical linear model</td>
</tr>
<tr>
<td>IM</td>
<td>inverted biological motion</td>
</tr>
<tr>
<td>PLDs</td>
<td>point-light displays</td>
</tr>
<tr>
<td>PLW</td>
<td>point light walker</td>
</tr>
<tr>
<td>pSTS</td>
<td>posterior superior temporal sulcus</td>
</tr>
<tr>
<td>SM</td>
<td>scrambled biological motion</td>
</tr>
<tr>
<td>TC</td>
<td>Talairach coordinates</td>
</tr>
<tr>
<td>TD</td>
<td>Typically developing</td>
</tr>
<tr>
<td>TDs</td>
<td>typically developing children</td>
</tr>
<tr>
<td>UM</td>
<td>upright biological motion</td>
</tr>
<tr>
<td>VEPs</td>
<td>visually evoked potentials</td>
</tr>
</tbody>
</table>
Table 2 (caption): Summary of studies on BM perception in ASD. (Neurophysiology findings are shown in bold. Abbreviations: dysf = finding of BM-processing dysfunction in ASD; HFA = high functioning autism; ID = intellectual disability; PLW = PLD of walking human; PLA = PLD of diverse human actions; PLO = PLD of inanimate object motion; SpSM = spatially scrambled PLD; PhSM = phase-scrambled PLD; IN = in noise; CM = coherent motion; MJ = minimum jerk; FC = forced choice; DD = direction detection; FFM = form-from-motion; hypo = hypoactivation of hemodynamic response in participants with ASD in brain areas; R = right; STS = superior temporal sulcus; STG = superior temporal gyrus; ACG = anterior cingulate gyrus; PCG = postcentral gyrus; IPL = inferior parietal lobule; occ = occipital areas; FG = frontal gyri; FFG = fusiform gyrus; claus = claustrum; dIPFC = dorsolateral prefrontal cortex; vPFC = ventral prefrontal cortex; ◊ = result not conclusive).
Table 2:
<table>
<thead>
<tr>
<th>Paper</th>
<th>Dx(N)</th>
<th>ages</th>
<th>stimuli</th>
<th>task</th>
<th>dysf</th>
<th>ASD findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annaz et al. (2010)</td>
<td>Aut?(23)</td>
<td>5-12</td>
<td>1. PLA vs. PhSM</td>
<td>FC</td>
<td>Y</td>
<td>d': flat developmental trajectories; BM detection threshold diff. not correlated with &amp; greater than CM &amp; FFM diff.</td>
</tr>
<tr>
<td>Annaz et al. (2012)</td>
<td>ASD(17)</td>
<td>3-7</td>
<td>1. PLA vs. PhSM</td>
<td>Monitored fixation time on dual displays</td>
<td>Y</td>
<td>atypical lack of preference for PLA over PS; atypical preference for PLO</td>
</tr>
<tr>
<td>Atkinson (2009)</td>
<td>Aut(1) AS(12)</td>
<td>17-58</td>
<td>PLA</td>
<td>FC labeling</td>
<td>Y</td>
<td>less accuracy</td>
</tr>
<tr>
<td>Blake et al. (2003)</td>
<td>Aut(12)</td>
<td>ASD:8-10 TD:5-10</td>
<td>PLA</td>
<td>Simple categorization task</td>
<td>Y</td>
<td>d': correlated with disorder severity</td>
</tr>
<tr>
<td>Castelli et al. (2002)</td>
<td>HFA/AS(10)</td>
<td>ASD:33(8) TD:25(5)</td>
<td>animate triangles</td>
<td>Verbal descriptions</td>
<td>Y</td>
<td>impaired mentalizing; hypo: mPFC, STS, temporal poles; extrastriate-STS conn.</td>
</tr>
<tr>
<td>Congiu et al. (2010)*</td>
<td>HFA(19)</td>
<td>ASD:8-19 TD:8-9</td>
<td>non-rigidly moving shapes</td>
<td>Verbal descriptions</td>
<td>(Y)</td>
<td>Less likely to ascribe animacy at least with prompting</td>
</tr>
<tr>
<td>Cook et al. (2009)*</td>
<td>ASD(16)</td>
<td>ASD:34(12) TD:33(12)</td>
<td>MJ hand and gravitational ball to constant velocities</td>
<td>judging &quot;less natural&quot;</td>
<td>(Y)</td>
<td>atypical lack of increased sensitivity to MJ</td>
</tr>
<tr>
<td>Freitag et al. (2008)</td>
<td>ASD(15)</td>
<td>ASD:18(4) TD:19(1)</td>
<td>PLW vs. constant velocity SpSM</td>
<td>1. fMRI task: &quot;later report&quot; 2. behavioral: 2AFC? Categorization</td>
<td>Y</td>
<td>longer RTs (same ERs); hypo: R: MTG near STS, PCG, IPL, occ, medial FG, middle FG; L: ant STG, FFG, PCG, IPL, claus</td>
</tr>
<tr>
<td>Herrington et al. (2007)</td>
<td>AS</td>
<td>ASD:28 (7) TD:26 (5)</td>
<td>PLW vs. vertically scrambled</td>
<td>DD</td>
<td>(N)</td>
<td>ceiling levels for PLW; asymmetric hypo: bilat. cerebellum, FF, STG and angular gyr, etc. for PLW; no interaction</td>
</tr>
<tr>
<td>Hubert et al. (2007)</td>
<td>HFA(4) AS (15)</td>
<td>15-34</td>
<td>PLA</td>
<td>Verbal descriptions</td>
<td>N</td>
<td>emotion-from-BM impairment only</td>
</tr>
<tr>
<td>Jones et al. (2011)</td>
<td>ASD</td>
<td>14-17</td>
<td>PLW IN vs. PhSM</td>
<td>“Point to person”</td>
<td>(N)</td>
<td>better at MC, worse at FFM &amp; BM - not sig? low IQ ASD - BM deficit; BM correlation w/ToM</td>
</tr>
<tr>
<td>Kaiser et al. (2010a)</td>
<td>HFA(3); AS(2); PDD-NOS(1)</td>
<td>ASD:20 (10); TD: 21(4); Un/-Masked/SM: PLA vs. PLO</td>
<td>FC detection</td>
<td>(Y)</td>
<td>d': no enhanced sensitivity to BM relative to non-BM</td>
<td></td>
</tr>
<tr>
<td>Kaiser et al. (2010b)</td>
<td>ASD</td>
<td>4-18</td>
<td>PLA vs. LS</td>
<td>no task</td>
<td>N/A</td>
<td>Hypo: pSTS, vPFC, FG, and amyg.; correl between R pSTS and SRS scores</td>
</tr>
<tr>
<td>Klin &amp; Jones (2008)</td>
<td>Aut (1)</td>
<td>1.25</td>
<td>PLAs</td>
<td>eye tracking (2AFC)</td>
<td>Y</td>
<td>no preference for BM</td>
</tr>
<tr>
<td>Klin et al. (2009)</td>
<td>ASD (21) delayed (16)</td>
<td>2</td>
<td>PLA UM vs. IM</td>
<td>eye tracking (2AFC)</td>
<td>Y</td>
<td>no preference for UM except w/audiovisual synchrony</td>
</tr>
<tr>
<td>Study (Year)</td>
<td>Group</td>
<td>Sample Size</td>
<td>Task</td>
<td>Condition</td>
<td>Outcome</td>
<td>Note</td>
</tr>
<tr>
<td>-------------</td>
<td>-------</td>
<td>-------------</td>
<td>------</td>
<td>-----------</td>
<td>---------</td>
<td>------</td>
</tr>
<tr>
<td>Koldewyn et al. (2010)</td>
<td>Aut(26) AS(3)</td>
<td>11-20</td>
<td>PLW IN</td>
<td>DD</td>
<td>Y</td>
<td>higher thresholds; hypo: pSTS, parietal, and frontal; dIPFC inv. related to severity</td>
</tr>
<tr>
<td>Koldewyn et al. (2011)</td>
<td>Aut(13) AS(3)</td>
<td>11-20</td>
<td>PLW IN</td>
<td>DD</td>
<td>Y</td>
<td>higher thresholds; for both conditions: smaller and earlier P100 in cASD; N200 R dominance only in TDs</td>
</tr>
<tr>
<td>Kroger et al. (2011)</td>
<td>ASD(3)</td>
<td>11-20</td>
<td>PLW vs. SpSM</td>
<td>2AFC</td>
<td>N</td>
<td>hypo: pSTS, parietal, and frontal; dIPFC inv. related to severity</td>
</tr>
<tr>
<td>McKay et al. (2012)</td>
<td>ASD</td>
<td>18-38</td>
<td>PLWs and partially scrambled PLWs</td>
<td>DD</td>
<td>N</td>
<td>similar thresholds; separate form &amp; motion pathways vs. temporoparietal in TD</td>
</tr>
<tr>
<td>Moore et al. (1997)</td>
<td>ASD:11-19 ID:10-18</td>
<td>1.PLW; 2.PLA</td>
<td>categorized</td>
<td>N</td>
<td>only emotion- and mental-state-from-BM impairment</td>
<td></td>
</tr>
<tr>
<td>Murphy et al. (2009)</td>
<td>ASD:26(8) TD:26(3)</td>
<td>Translating PLW vs SpSM IN</td>
<td>2AFC DD</td>
<td>N</td>
<td>UM faster RT than SM, as in TD</td>
<td></td>
</tr>
<tr>
<td>Nackaerts et al. (2012)</td>
<td>ASD:35(9) TD:32(6)</td>
<td>headless, emotional PLAs vs. SpSM</td>
<td>1. 2AFC person/not; 2. emotion recognition</td>
<td>Y</td>
<td>BM ability related to emotion recogn. but didn’t entirely explain emotion deficit; saccade diffs</td>
<td></td>
</tr>
<tr>
<td>Parron et al. (2008)</td>
<td>ASD:12(3) TD:12(2)</td>
<td>PLA</td>
<td>Verbal descriptions</td>
<td>N</td>
<td>deficits specific to the detection of emotion</td>
<td></td>
</tr>
<tr>
<td>Price et al. (2009)</td>
<td>AS</td>
<td>8-23</td>
<td>Leg PLDs</td>
<td>gait typicality discrimination</td>
<td>Y</td>
<td>decreased sensitivity in AS</td>
</tr>
<tr>
<td>Rutherford &amp; Troje (2011)</td>
<td>ASD:29(6) TD:31(9)</td>
<td>PLW, cat, and pigeon vs. SpSM with 1. SpSM mask, 2. flickering mask</td>
<td>1. 2AFC detection of coherent PLD IM; 2. DD</td>
<td>N</td>
<td>correlation with IQ in ASD; no better at DD in humans than animals (best at pigeons?) as opposed to TD; high IQ ASD more affected by SM, less by IM</td>
<td></td>
</tr>
<tr>
<td>Saygin et al. (2010)</td>
<td>ASD:34(14)</td>
<td>PLW IN</td>
<td>FC DD</td>
<td>N</td>
<td>comparable psychophysical thresholds</td>
<td></td>
</tr>
<tr>
<td>Swettenham et al. (2012)</td>
<td>ASD:10(2) TD:9(2)</td>
<td>pointing PLD cue</td>
<td>Posner paradigm</td>
<td>(Y)$^5$</td>
<td>RTs not faster- for valid PLD direction cues</td>
<td></td>
</tr>
<tr>
<td>Weisberg et al. (2012)</td>
<td>HFA</td>
<td>12-24</td>
<td>human/tool</td>
<td>category decision task</td>
<td>(N)$^5$</td>
<td>&gt;90% correct; (dynamic) People&gt;tools (and social&gt;mechanical) in R lat. FFG only in TDs; less conn. with pSTS &amp; amyg.</td>
</tr>
</tbody>
</table>
Table 3: Mean ages and IQs of the two cohorts of children used in the study.

<table>
<thead>
<tr>
<th>Groups</th>
<th>N (female)</th>
<th>Age in yrs.</th>
<th>VIQ</th>
<th>PIQ</th>
<th>FSIQ</th>
<th>AS, autism</th>
</tr>
</thead>
<tbody>
<tr>
<td>cASD</td>
<td>35 (4)</td>
<td>10.48 (2.27)</td>
<td>7.1-15.7</td>
<td>101.66 (22.47)</td>
<td>108.26 (18.54)</td>
<td>105.40 (21.26)</td>
</tr>
<tr>
<td>TDs</td>
<td>46 (22)</td>
<td>11.22 (2.90)</td>
<td>6.1-16.9</td>
<td>116.59 (14.26)</td>
<td>108.24 (12.88)</td>
<td>113.98 (13.87)</td>
</tr>
</tbody>
</table>
Table 4: Mean behavioral scores for the two groups.

<table>
<thead>
<tr>
<th>means (SD)</th>
<th>cASD</th>
<th>TDs</th>
</tr>
</thead>
<tbody>
<tr>
<td>UM d'</td>
<td>1.20 (1.05)</td>
<td>1.81 (0.98)</td>
</tr>
<tr>
<td>IM d'</td>
<td>0.92 (0.88)</td>
<td>1.27 (0.83)</td>
</tr>
<tr>
<td>SM d'</td>
<td>1.04 (0.94)</td>
<td>1.50 (0.85)</td>
</tr>
<tr>
<td>UM misses</td>
<td>0.05 (0.05)</td>
<td>0.05 (0.09)</td>
</tr>
<tr>
<td>IM misses</td>
<td>0.06 (0.07)</td>
<td>0.06 (0.09)</td>
</tr>
<tr>
<td>SM misses</td>
<td>0.08 (0.08)</td>
<td>0.08 (0.10)</td>
</tr>
</tbody>
</table>
Table 5: Results of the statistical analyses of behavioral scores for the two groups, with covariates of age, sex, and IQ. (*significant for α=0.05)

<table>
<thead>
<tr>
<th></th>
<th>d'</th>
<th>miss rates</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LSM diff</td>
<td>F</td>
<td>p</td>
<td></td>
<td></td>
<td>F</td>
<td>p</td>
<td></td>
</tr>
<tr>
<td>UM</td>
<td>group</td>
<td>0.751142</td>
<td>0.98</td>
<td>0.3258</td>
<td>0.03</td>
<td>0.8687</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>age</td>
<td>12.05682</td>
<td>15.72</td>
<td>0.0002*</td>
<td>0.61</td>
<td>0.4368</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>sex</td>
<td>0.838309</td>
<td>1.09</td>
<td>0.2994</td>
<td>0.03</td>
<td>0.855</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>fsiq</td>
<td>6.624557</td>
<td>8.64</td>
<td>0.0044*</td>
<td>0.28</td>
<td>0.6006</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IM</td>
<td>group</td>
<td>0.00497</td>
<td>0.01</td>
<td>0.9248</td>
<td>0.05</td>
<td>0.8286</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>age</td>
<td>7.629351</td>
<td>13.77</td>
<td>0.0004*</td>
<td>0.54</td>
<td>0.4666</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>sex</td>
<td>1.048358</td>
<td>1.89</td>
<td>0.1733</td>
<td>0.00</td>
<td>0.9862</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>fsiq</td>
<td>4.096876</td>
<td>7.39</td>
<td>0.0082*</td>
<td>0.18</td>
<td>0.6687</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SM</td>
<td>group</td>
<td>0.205966</td>
<td>0.34</td>
<td>0.5602</td>
<td>0.04</td>
<td>0.8336</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>age</td>
<td>9.186129</td>
<td>15.28</td>
<td>0.0002*</td>
<td>0.5</td>
<td>0.4834</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>sex</td>
<td>0.773127</td>
<td>1.29</td>
<td>0.2606</td>
<td>0.00</td>
<td>0.9466</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>fsiq</td>
<td>4.85618</td>
<td>8.08</td>
<td>0.0058*</td>
<td>0.22</td>
<td>0.6408</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 6: Results of the initial GLM average-amplitude analysis. Entries are the $P$-values for the areas-under-the-curves of the designated time-windows over the selected ROIs (PO7, PO8). (*significant for an alpha-criterion of 0.05)

<table>
<thead>
<tr>
<th></th>
<th>P1</th>
<th>N1</th>
<th>P2</th>
<th>N2</th>
<th>P3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>129-159 ms</td>
<td>200-230 ms</td>
<td>250-300 ms</td>
<td>300-350 ms</td>
<td>350-500 ms</td>
</tr>
<tr>
<td>group</td>
<td>0.0023*</td>
<td>&lt;.0001*</td>
<td>&lt;.0001*</td>
<td>&lt;.0001*</td>
<td>&lt;.0001*</td>
</tr>
<tr>
<td>task</td>
<td>0.7825</td>
<td>0.0456*</td>
<td>0.0603</td>
<td>0.2748</td>
<td>0.4109</td>
</tr>
<tr>
<td>group*task</td>
<td>0.9796</td>
<td>0.9642</td>
<td>0.6496</td>
<td>0.7347</td>
<td>0.9365</td>
</tr>
<tr>
<td>mot</td>
<td>0.7194</td>
<td>0.2436</td>
<td>0.0039*</td>
<td>0.0005*</td>
<td>0.0067*</td>
</tr>
<tr>
<td>group*mot</td>
<td>0.9903</td>
<td>0.9268</td>
<td>0.9178</td>
<td>0.982</td>
<td>0.9962</td>
</tr>
<tr>
<td>task*mot</td>
<td>0.9977</td>
<td>0.9765</td>
<td>0.8993</td>
<td>0.9401</td>
<td>0.9555</td>
</tr>
<tr>
<td>group<em>task</em>mot</td>
<td>0.9995</td>
<td>0.9877</td>
<td>0.9711</td>
<td>0.9529</td>
<td>0.9948</td>
</tr>
<tr>
<td>hemi</td>
<td>0.209</td>
<td>0.2256</td>
<td>0.0935</td>
<td>0.2612</td>
<td>0.2238</td>
</tr>
<tr>
<td>group*hemi</td>
<td>0.875</td>
<td>0.6703</td>
<td>0.8252</td>
<td>0.382</td>
<td>0.013*</td>
</tr>
<tr>
<td>task*hemi</td>
<td>0.8682</td>
<td>0.7824</td>
<td>0.8457</td>
<td>0.902</td>
<td>0.9663</td>
</tr>
<tr>
<td>group<em>task</em>hemi</td>
<td>0.9301</td>
<td>0.8606</td>
<td>0.9329</td>
<td>0.969</td>
<td>0.9665</td>
</tr>
<tr>
<td>mot*hemi</td>
<td>0.9905</td>
<td>0.9667</td>
<td>0.9128</td>
<td>0.9734</td>
<td>0.9895</td>
</tr>
<tr>
<td>group<em>mot</em>hemi</td>
<td>0.9676</td>
<td>0.9806</td>
<td>0.9865</td>
<td>0.963</td>
<td>0.9854</td>
</tr>
<tr>
<td>task<em>mot</em>hemi</td>
<td>0.9907</td>
<td>0.9895</td>
<td>0.9941</td>
<td>0.9924</td>
<td>0.9887</td>
</tr>
<tr>
<td>group<em>task</em>mot*hemi</td>
<td>0.9849</td>
<td>0.9984</td>
<td>0.9864</td>
<td>0.9916</td>
<td>0.98</td>
</tr>
<tr>
<td>age</td>
<td>&lt;.0001*</td>
<td>&lt;.0001*</td>
<td>&lt;.0001*</td>
<td>0.4043</td>
<td>&lt;.0001*</td>
</tr>
<tr>
<td>sex</td>
<td>&lt;.0001*</td>
<td>&lt;.0001*</td>
<td>&lt;.0001*</td>
<td>&lt;.0001*</td>
<td>&lt;.0001*</td>
</tr>
<tr>
<td>fsiq</td>
<td>&lt;.0001*</td>
<td>&lt;.0001*</td>
<td>0.0189*</td>
<td>0.0303*</td>
<td>0.1394</td>
</tr>
</tbody>
</table>
Table 7: Results of the 2\textsuperscript{nd} stage, expanded ROI group\texttimes motion-type HLM analysis. (Shown are uncorrected \(p\)-values that reached significance for an alpha criterion of 0.05 after Hochberg corrections [Hochberg, 1988].)

<table>
<thead>
<tr>
<th>comp</th>
<th>ms</th>
<th>elec</th>
<th>LSM diff</th>
<th>Cohen's d</th>
<th>(t)</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>unattended task</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N1'</td>
<td>200-250</td>
<td>P8</td>
<td>0.767</td>
<td>0.4833</td>
<td>3.31</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PO8</td>
<td>1.0188</td>
<td>0.4444</td>
<td>3.05</td>
<td>0.0024</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P6</td>
<td>0.6605</td>
<td>0.4162</td>
<td>2.85</td>
<td>0.0044</td>
</tr>
<tr>
<td>P2</td>
<td>250-300</td>
<td>P8</td>
<td>0.6452</td>
<td>0.3432</td>
<td>2.35</td>
<td>0.0189</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PO8</td>
<td>0.8414</td>
<td>0.3308</td>
<td>2.27</td>
<td>0.0237</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>attended task</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N1'</td>
<td>200-250</td>
<td>PO8</td>
<td>1.3897</td>
<td>0.397</td>
<td>2.72</td>
<td>0.0067</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P6</td>
<td>0.6458</td>
<td>0.3637</td>
<td>2.49</td>
<td>0.0128</td>
</tr>
<tr>
<td>P2</td>
<td>250-300</td>
<td>P7</td>
<td>1.1646</td>
<td>0.5104</td>
<td>3.5</td>
<td>0.0005</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P5</td>
<td>0.9773</td>
<td>0.4283</td>
<td>2.94</td>
<td>0.0034</td>
</tr>
</tbody>
</table>
Figure 1 (caption): A. Sequences of frames from sample clips of upright biological motion (UM), inverted biological motion (IM), and scrambled biological motion (SM). B. Components used in the stage one analysis as overlayed over the two analyzed bilateral parieto-occipital sites (PO7 and PO8), collapsed across all groups (cASD and TDs), conditions (UM, SM, and IM), and tasks (unattended and attended).
Figure 1:

A.

B.
Figure 2 (caption): VEPs for the unattended task for selected sites across the scalp for the two groups.
Figure 2:

Unattended

TDs

cASD

20 μV
200 ms

PO3  Fz  PO4
PO7  PO8
P9  Oz  P10

SM  IM  UM
**Figure 3 (caption):** VEPs for the attended task for the two groups for selected sites across the scalp.
Figure 3:
**Figure 4:** VEPs for the two groups collapsed across motion-types (UM, IM, SM) and tasks (unattended, attended.)
Figure 5 (caption): Scalp electrophysiology for the upright (UM) and scrambled motion (SM) stimuli, collapsed across both tasks (unattended and attended), as well as the difference between them, for both cASD and TDs, at the midpoints of the key components (posterior view; red = positive amplitude; blue = negative). Motion-type effects are seen bilaterally as amplified negativity from P2 (275 ms) onward over occipitotemporal sites, and are virtually indistinguishable between the two groups (TDs and cASD).
Figure 5:
Figure 6: Scalp topographies and VEPs that reached significance in the HLM analysis after Hochberg corrections for the 200-250 ms time-window. (Site P8 only reached significance after corrections for the unattended task but is included for illustrative purposes for the attended task as well.)
Figure 7: Scalp topographies and VEPs that reached significance in the HLM analysis after Hochberg corrections for the 250-300 ms time-window.
CHAPTER IV

GENERAL DISCUSSION

FROM PERCEPTS TO PERSONS: BIOLOGICAL MOTION

PROCESSING AND THEORY OF MIND
"They were so far away that they looked like dolls. They made her think of the way she imagined the people when she played Town. Somehow this way she could see them better than she ever had before. She looked at them carefully in the longish time it took them to reach her. She made herself walk in Sport's shoes, feeling the holes in his socks rub against his ankles. She pretended she had an itchy nose when Janie put one abstracted hand up to scratch. She felt what it would feel like to have freckles and yellow hair like Janie, then funny ears and skinny shoulders like Sport."

(Louise Fitzhugh, *Harriet the Spy* p. 297)
The experiments in this paper demonstrated an innate yet evolving, fundamental neuronal system devoted to the processing of biological motion (BM). In typical adults, BM processing consisted of three phases: an early (100-200 ms), task-invariant, right-lateralized occipito-temporal activation; a mid-level (200 to 350 ms), bilateral, posterior middle temporal activation that was amplified by attention; and a later (400- ms), centro-parietal activation that only occurred when BM was actively attended (see Chapter II).

This mature, hierarchical system contrasted strikingly with the neurophysiological responses of school-age children where BM stimuli elicited one wave of parieto-occipital neurophysiological activation that was unaffected by attentional task and that was only statistically significant from 250 ms onward (see Chapter III Section 2A). While BM perception is clearly innate, in typical, healthy development it continues to mature through childhood such that, by adulthood, BM-sensitive attentional resources are sensitive to explicit intentions.

Children with autism spectrum disorders (ASD; see chapter III) demonstrated an ability at BM detection comparable to that of typically developing children, as measured by d-prime scores. They also exhibited a relatively typical electrophysiological differentiation between BM stimuli, regardless of attentional task. While large neurophysiological group differences emerged in our initial analysis, they did so consistently for all three motion types (upright BM, inverted BM, and scrambled BM), and were therefore suggestive of general complex motion processing dysfunctions (see Chapter III Section 2A), or even general visual processing differences (see e.g. Brandwein et al., 2013).
A more powerful follow-up analysis, however, revealed neurophysiological abnormalities specific to BM differentiation from 200 to 300 ms (see Chapter III Section 2B). This finding was consistent with recent neuroimaging findings that found BM neural processing differences in ASD (see e.g. Freitag et al., 2008; Herrington et al., 2007; Kaiser et al., 2010; Koldewyn et al., 2011) and lent credence to a model of ASD where social dysfunctions, such as in empathy or theory-of-mind, have roots in early perceptual deficits. In what follows, we will attempt to flesh out a model of how social-perceptual processes such as BM lead up to higher order social cognitive functions such as theory-of-mind, as well as how they can then be implicated in social-cognitive dysfunctions such as in ASD.

**BIOLOGICAL MOTION AND THEORY-OF-MIND**

Theory-of-mind refers to the ability to form a mental representation of another's desires, beliefs, emotions, and cognitive state (see e.g. Premack and Woodruff, 1978). This ability likely depends on what are referred to as “mirror neurons” and “mirror-neuron networks” (see e.g. Iacoboni and Depretto, 2006; Rizzolati and Craighero, 2004). These networks of cells are marked by activity in response both to the perception of one’s own actions, as well as to perceived actions of another. As we will explain, such a system ultimately can enable an association of overt, sensorially-observed behaviors with implicit cognitive, affective, and intentional states.

If early in development there is a disruption in the sensory processing that leads up to the interpretation of another, both the subject’s ability to functionally represent the
other, as well as the subject’s ability to represent itself can be compromised. This is because a child’s typical construction of concepts of “self” and “other” is bidirectional. That is to say, just as perception of one’s own internally perceived states informs perception of another’s, so too, an “outside” conceptualization of another sentient person informs self-awareness and self-perception.

In light of this, it is hardly surprising that pronoun usage is often implicated in ASD (see e.g. Carmody and Lewis, 2012; Lee, Hobson, and Chiat, 1994) as autistic children may suffer from theory-of-mind deficits that render the concepts of “you” and “me” particularly difficult to grasp. If a fundamental social-sensory stimulus such as biological motion or eye-gaze is processed abnormally, this can potentially lead to delays and impairments in the natural development of more sophisticated aspects of social cognition, such as theory-of-mind and empathy.

**DISCOVERING THE “OTHER”**

In constructing a sense of “self” and of “other”, a child or adult necessarily both interprets and distinguishes aspects that are both similar and dissimilar in the “other” relative to the “self”. While a newborn may engage in a solipsistic worldview where only its own desires and perceptions exist, the typical development of the recognition of other perspectives enables more advanced cognitive and affective levels of social interaction and engagement. In order for such a social-cognitive maturation to occur, there must be a discovery of commonality via a perceived similar impact on a shared world (see figures 1 and 2). This process can be mediated via inductive associations of
overtly observed behavior with internal cognitive, affective, and intentional states which would be intrinsically linked with an overlapped representation of “self” and “other”. The neural correlates of this social-cognitive phenomenon are arguably the aforementioned mirror neurons and mirror-neuron networks.

**BIOLOGICAL MOTION, MIRROR-NEURONS, AND THEORY-OF-MIND**

While there is still much work to be done mapping out the precise coordinates of these mirror-neuron networks, there is already substantial evidence that parieto-occipito-temporal sites may mediate self-vs.-other encoding (see e.g. David *et al.*, 2009; see also Saxe *et al.*, 2004; Pelphrey, Morris, and McCarthy, 2004; Vollm *et al.*, 2006; Hodzic *et al.*, 2009a; Hodzic *et al.*, 2009b). As such, it seems plausible that our findings in Chapter III of abnormal electrophysiological responses to BM stimuli in children with ASD near these sites may indicate the roots of a theory-of-mind deficit in ASD.

Considering that areas such as pSTS are activated both by canonical BM stimuli as well as in theory-of-mind paradigms (see e.g. Hein and Knight, 2008), it would seem plausible that at least some aspects of theory-of-mind mature to become an early and automatic neuronal function. Ultimately, however, social cognition is neither a simple process nor a simple concept and any serious attempt in mapping out the trajectory from visual stimulation to theory-of-mind necessitates some level of complexity. Going forward, we will explore a current model that addresses some of such social-cognitive complexity.
THE SYSTEMIZING-EMPATHIZING MODEL OF COGNITION

In a series of articles beginning in 2002, Dr. Simon Baron-Cohen proposed what had perhaps already been a "folk-psychology" generalization about neurocognitive differences between the sexes. According to Baron-Cohen’s model, people could be classified based on their ability to “empathize”, i.e. detect another’s internal emotional and intentional states and respond accordingly, as well as according to their ability to “systemize”, i.e. organize a complex system according to its rules enabling reliable predictions about its behavior (Baron-Cohen, 2002; see also Baron-Cohen, 2009). Baron-Cohen demonstrated that, on average, women were typically better “empathizers” than men, while men were, more often than not, better “systemizers” (see e.g. Baron-Cohen et al., 2003). This led him to additionally propose a corresponding sex-based model of ASD.

THE EXTREME MALE BRAIN MODEL OF AUTISM

In his “extreme male brain” model of ASD, an offshoot of the systemizing-empathizing model of human cognition, Baron-Cohen suggested that much of the symptoms of ASD can be explained as an over-expression of the male “systemizer” cognitive style (see e.g. Baron-Cohen et al., 2003; Baron-Cohen, 2009; Baron-Cohen et al., 2011; Brosnan, Gwilliam, and Walker, 2012; Teatero and Netley, 2013; see also, however, Beacher et al., 2012). Perhaps mediated by an over-exposure to fetal testosterone in utero (see Knickmeyer et al., 2006; see also Whitehouse et al., 2010; Aiello and Whitaker-Azmitia, 2011), and possibly via the genetic union of two high
(albeit nonclinical) “systemizers” (see Baron-Cohen, 2006), ASD was suggested to arise from a dysfunctional bias to “systemize” rather than “empathize”, resulting in an inability to function normally socially. While Baron-Cohen’s “systemizer-empathizer” and “extreme male brain” models have been shown to possess high explanatory power as well as substantial confirmation from multiple studies, they might perhaps still benefit from some clarification and reformulation, without damaging the core strengths of the models.

**THIRD-PERSON/FIRST-PERSON MODEL OF COGNITION**

An alternative way to formulate the “empathizer/systemizer” model might be as follows. There are two ways to process information: via “third-person”, detached, categorical mechanisms or via “first-person”, empathetic, “self-oriented” mechanisms. In a third-person processing stream, objects are essentially inanimate and the processing for the most part is non-empathetic and merely predicts behavioral patterns within the system from an entirely external perspective. This would correspond to Baron-Cohen’s “systemizing”.

The first-person system, in contrast, relies heavily on the projection of internally perceived motivational and emotional information in interpreting and predicting externally perceived behaviors. The first-person system would be heavily associated with mirror neuron systems that are activated both by perceived self-initiated actions as well as perceived actions of others. Accordingly, it can also be related to altruistic behavior in as much as altruism reflects a level of identification with a perceived other.
Such a system would correspond to Baron-Cohen’s “empathizing”. Such a “1st-Person/3rd-Person” reformulation arguably broadens the sweep of Baron-Cohen’s model and more directly accounts for the aforementioned, strikingly specific language impairments in ASD related to appropriate “1st-person” vs. “3rd-person” pronoun use (see e.g. Carmody and Lewis, 2012; Lee, Hobson, and Chiat, 1994).

It is premature to conclusively map out the neurophysiology of such dual systems. However, considering that there do appear to be right-hemisphere biases toward emotion processing (see e.g. Blonder, Bowers, and Heilman, 1991), hemispheric lateralization might be a prime candidate for a crude model of such a dual social-cognitive neural system. Considering the aforementioned enhanced emotion-processing abilities in females compared to males (see e.g. Schulte-Rüther et al., 2008), our findings of reduced “N1′” (200-250 ms) amplifications in cASD exclusively over the right hemisphere (see Chapter II Section 2) are arguably suggestive of the right-lateralized half of this component’s role in a potentially empathetic processing of biological motion. In light of the source localization findings in adults reported in Chapter II regarding the N250, it seems likely that this component includes activity from the posterior superior temporal sulcus (pSTS), which has been potentially associated with processing distinctions between the visually represented “self” and “other” (see e.g. Kontaris, Wiggett, and Downing, 2009), a distinction that is at the core of theory-of-mind.

Nonetheless, as for instance evidenced by our left-lateralized P2 (250-300 ms) group effect for the explicit BM-detection task, BM-processing dysfunction in ASD is not simply a right-brain, affective disorder. Bilateral configural BM representation appears
to be implicated in ASD. This points not only to the potential complexity of ASD, but to our still impoverished understanding of hemispheric lateralization and social processing in general.

Hopefully, future research will fill in the gaps and inform more potent theoretical and clinical social-cognitive models, yielding both a greater understanding of the “basic science” of “normal” social cognition, as well new and more powerful clinical treatments of social cognitive dysfunctions such as ASD. For example, by making use of neuroplasticity, one could envision targeted training of the “3rd-person”/“systemizing” system to compensate for deficits in “1st-person” empathizing.

CONCLUSION

Biological motion (BM) processing, while innate and present from birth, is nonetheless a dynamic and complex set of processes that continues to mature throughout the school-age years. In healthy, typical adults, BM processing includes an early, attentionally-invariant electrophysiological component (100-200 ms) not apparent in childhood/adolescence. In addition, a mid-level component (200-350 ms) that is extant already in childhood is only amplified by attention in adulthood, and a third, later component (450+ ms) also only appears in the mature brain.

It is quite plausible that a deficit in the substantial attentional tuning that occurs in childhood plays a role in the social dysfunctions of the autism spectrum disorders (ASD). Most notably, right temporo-occipital “N1” (200-250 ms) amplification seen in typical development are dampened in ASD. This finding may lend support to a model of
social cognition whereby lateralized, complex, parallel processing of visual stimuli is healthily interpreted both in a “3rd-person” stream primarily in left regions as well as in a “1st-person” stream primarily in the right hemisphere. ASD include a specific “1st-person” processing deficit that underlies much of the social dysfunctions associated with the disorders. Future research will continue to unravel the complexity of these processes and may yield new clinical applications of this model such as the recruitment of canonical “systemizing” regions in “1st-person” processes in those with ASD.
CHAPTER IV: DISCUSSION – FIGURES
**Figure 1:** A symbolic representation of a model of social-cognition whereby perception of a medium shared by self and other involves inductive association, as well as differentiation, of socially produced events. The interactive medium represents the shared environment where 0s and 1s represent values manipulated via the motor output of two interacting minds. By comparing manipulations perceived (via sensory input) as self-generated biological motions with those that are not perceived as self-generated, the social observer can detect and construct a sense of the both similar and dissimilar “other”.
Figure 2: A very simplified model of social cognition where BM of self and of other is extracted and segregated from the environment and is used in the construction of a theory of mind.
REFERENCES


Chang D. H., Troje N. F. Acceleration carries the local inversion effect in biological


Frey H. P., Molholm S., Lalor E. C., Russo N. N., Foxe J. J. Atypical cortical representation of peripheral visual space in children with an autism spectrum
Hirai M., Watanabe S., Honda Y., and Kakigi R. Developmental changes in point-light


Koldewyn K., Whitney D., Rivera S. M. The psychophysics of visual motion and global
Koldewyn K., Whitney D., Rivera S. M. Neural correlates of coherent and biological
Kozlowski, L. T. & Cutting, J. E.. Recognizing the sex of a walker from a dynamic point-
neurophysiology of human biological motion processing: A high-density electrical
Kröger A, Bletsch A, Krick C, Siniatchkin M, Jarczok TA, Freitag CM, Bender S.
Visual event-related potentials to biological motion stimuli in autism spectrum

Lepage J. F. and Théoret H. EEG evidence for the presence of an action observation–
execution matching system in children. European Journal of Neuroscience 23
Lord C., Rutter M., Le Couteur A. Autism Diagnostic Interview-Revised: a revised
version of a diagnostic interview for caregivers of individuals with possible
Lord C., Risi S., Lambrecht L., Cook E. H. J., Leventhal B. L., DiLavore P. C., Pickles A.
& Rutter M. The autism diagnostic observation schedule-generic: a standard
measure of social and communication deficits associated with the spectrum of
Mather G., Murdoch L. Gender discrimination in biological motion displays based on
Mather G., Radford K., West S. Low-level visual processing of biological motion. Proc
McKay L. S., Simmons D. R., McAleer P., Dominic Marjoram, Piggot J., Pollick F. E. Do
distinct atypical cortical networks process biological motion information in adults


Pellicano, E., Gibson, L., Maybery, M., Durkin, K., & Badcock, D. R. Abnormal global processing along the dorsal visual pathway in autism: A possible mechanism for


Vollm, B. A., Taylor, A. N.W., Richardson, P., Corcoran, R., Stirling, J., McKie, S.,
