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On the Brainstem Origin of Autism: Disruption to Movements of the Primary Self

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Abstract

This paper examines evidence for a disorder of the intrinsic motive processes of the purposeful self in autism spectrum disorder (ASD), which leads to weakening of shared experience in early childhood. Changed motor and affective regulations that identify autism are traced to faults in neurogenesis in the core brainstem systems of the fetus. These fundamental systems have evolved to serve development of sensory guidance for motor activity and affective regulation of projects of thought and action, including communication of intentions and feelings with other human selves.

Affective neuroscience describes subcortical organs in mammals that are responsible for the coherence of a primary conscious self-as-agent, with emotions that communicate feelings for selective sociability with other individuals. In humans this affective consciousness is adapted as the foundation for active engagement of an infant with a world of objects and people by expressions under the control of shared rhythms of an 'intrinsic motive pulse'. We give primary importance to the disorder in autism of the accuracy of

timing in this resonant central nervous system, responsible for coordination of movement with companions. We relate this understanding of the disorder to problems in the monitoring of prospective regulation of actions of the conscious Self by a body-related affective valence, which affects the arousal of personal satisfaction of purposes or anxiety at their failure, and engagement in affectionate or antagonistic relations. This leads to evaluation of participation in movements with shared feelings for therapy and teaching to helping the socio-emotional development and learning of children with autism, as well as advice for lifetime care.

In autism, the essential embodiment of early childhood experience for growth of knowledge, skill and collaborative social understanding appears weakened by a sensorimotor deficit in motivation and its affective control. This has life-long developmental consequences, affecting the intersubjective responses of family, and then cooperative attentions of companions and teachers in the community. Mis-coordination of movements leads to frustration, distress, and anxiety, creating social withdrawal and avoidance, or over-compensations expressed as increased arousal and hyper-activity. Indeed, we propose that disabilities in cognitive intelligence and language are secondary to weakness in prospective control of movements with affective appraisal of anticipated experiences.

We identify the origin of these symptoms in disorders of brainstem mechanisms that develop in the late embryo stage and that are essential for motor and affective regulations, as well as autonomic processing. In particular, data indicate an anatomical and functional disruption of the inferior olive, associated with control of motor timing by the cerebellum, and abnormal development of the neighbouring nucleus ambiguus, involved in expressions of social engagement and speech. These nuclei appear to be critical components of the core neuropsychological system that develops abnormally to produce the varied autistic spectrum disorders.

We draw attention to the limitations of research methods in neuroscience and psychology that seek to identify a primary cognitive, information-processing and neocortically mediated disorder by testing the response of the individual in artificial situations. New research using micro-kinesic descriptive methods clarifies motor deficits that characterize autism. Furthermore, extensive imaging of brain activities supports a philosophical psychology of embodiment that elucidates how confusion in unconscious prospective control of actions from fetal stages impairs the child's developing subjective agency. Finally, we offer information on movement-based therapies that can help to facilitate learning, self-regulation, and pleasure in social interaction for individuals with ASD.

INTRODUCTION: MOTOR CONTROL OF THE EMBODIED SELF MEDIATES AUTOPOESIS OF CONSCIOUS EXPERIENCE, AND ITS CONSENSUAL SHARING

Characteristics of Prospective Control of Movement

Movement is the generator and regulator of animate experience. An animal can engage effectively with the world and explore its properties only through muscle activity that is regulated purposefully in body-related time and space (Llinás 2001), and with affective appraisal of its risks and benefits (Panksepp 2005; Packard and Delafield-Butt 2014).

Movement of the human body, with its elaborate adaptations for communication of interests and feelings, holds properties essential to the psychological well-being of the individual as a whole Self, and for generating opportunities for social cooperation and affording perceptual information for learning, sharing, and elaboration of conscious skill and knowledge (Condon 1975b, 1979, Trevarthen, Gratier, and Osborne 2014, Trevarthen 2001). Two essential life functions defined by the systems theorist Humberto Maturana as ‘autopoesis’, or ‘self-making’, and ‘consensuality’, the constructive collaboration of vital individuals, be they cells in tissues and organs, or individuals in viable social or cultural groups (Maturana, Mpodozis, and Carlos Letelier 1995, Maturana and Varela 1980; Packard and Delafield-Butt, 2014), are affected in varying degrees by changed brain development in individuals with ASD.

Normal human movements are prospectively controlled (von Hofsten 2007, Lee 2009) to constitute a basic subjective intentionality or core mental state of the individual-as-agent from early fetal life (Delafield-Butt and Trevarthen 2013, Delafield-Butt and Gangopadhyay 2013). Passive, reactive reflex corrections only occur in an unanticipated emergency. Accumulated evidence in prenatal stages of human development demonstrate fetal movements are controlled in body-related time and space as pre-reflective intentions – active generators and regulators of experience and expressive of emotions (Lecanuet et al. 1995, Reissland et al. 2014, Reissland, Francis, and Mason 2013, Piontelli 1992, Zoia et al. 2007, Delafield-Butt and Gangopadhyay 2013). Movement, as the physical expression of our psychological being, manifests our intentions and expresses our feelings in the nuances of body posture, composure and composition, and in the 'forms of its vitality' of gestures in shared social space (Stern 2010). Whether we wish them to do so or not, movements communicate our intentions to others in gesture, speech, in symbols and in the imaginative projects that we create in any activity, privately, in intimate relations, or in public (Baldwin 1895, Trevarthen, Delafield-Butt, and Schögler 2011). They convey 'the human seriousness of play' (Turner 1982), sharing the passions by which we regulate social cooperation and the creation of cultural conventions of education, religion, art and technique (Trevarthen, Gratier and Osborne 2014; Delafield-Butt and Adie 2016).

Disrupted Movements in Autism

It has become increasingly clear over the last decade that ASD is characterized by a disruption to motor coordination and timing (Trevarthen et al. 1998, Trevarthen 2000, Trevarthen and Daniel 2005, Trevarthen and Delafield-Butt 2013a). Since Teitelbaum and colleagues' paper in 1998 (Teitelbaum et al. 1998) that showed poor posture and coordination of the limbs in a retrospective video analysis of newborns who later developed autism, a growing field of research is measuring and characterising motor deficits (Torres and Donnellan 2013, Fournier et al. 2010). Motor skills are disrupted in toddlers with autism, not simply delayed, and this motor disturbance becomes exacerbated over the first years of life (Lloyd, MacDonald, and Lord 2013). The cause of this deficit in motor kinesics and its place in the development of autism is fundamental for understanding the aetiology of the condition, and for planning treatment (Condon and Ogston 1966, Condon 1975a).

Motor control research in the last decade demonstrates that the kinematics of components of action in tasks as varied as making simple horizontal arm movements (Cook, Blakemore, and Press 2013), reaching (Sacrey et al. 2014), reaching-and-grasping (Stoit et al. 2013), arm movements to goals (Dowd et al. 2012), and handwriting (Kushki, Chau, and Anagnostou 2011) are disturbed in individuals with autism. These are disturbances in goal-directed tasks that serve the intentions of the agent. Postural adjustments during load-shift tasks (Schmitz et al. 2003) and during gait (Rinehart et al. 2006) are affected. And efficient prospective organisation of movements in a series or chain of purposes is thwarted (Fabbri-Destro et al. 2009). Prospective, or feed-forward, mechanisms of motor timing appear fundamentally disrupted in autism (David et al. 2012). Perceptual awareness of others' intentions conveyed in body movement or in eye gaze is also weakened (Cattaneo et al. 2007, Pierno et al. 2006). A comprehensive meta-analysis of all motor data in autism revealed substantial motor coordination deficits pervasive across the spectrum of ASD diagnoses (Fournier et al. 2010). Motor disruption can be considered a core feature of autism.

The psychological upshot of the motor disruption in autism is a disruption to a principal form of *prospective motor agency* – the capacity to efficiently enact desired intentions through actions of the body (Trevarthen and Delafield-Butt 2013a, Delafield-Butt and Gangopadhyay 2013, Trevarthen 2016). Disruption to prospective motor timing leads to a disruption in successfully completing a desired intention, which in turn leads to anxiety and distress, and can create social isolation with its consequent autistic emotional avoidance and rejection as compensations. However, the subtle nature of the disruption in autism to prospective motor control and the means by which these features may be observed do not as yet allow for their inclusion in standard clinical diagnostic criteria (American Psychiatric Association 2013). We believe this will change as principles and methods of motor assessment become more accessible to clinicians (Anzulewicz, Sobota, and Delafield-Butt 2016) and the motor disruption in autism better understood by the clinical community.

Movement at the Root of Human Communication and Social Understanding

Efficient control of purposeful movement is necessary to communicate, to share intentions, and to generate shared meaning about the world. Human meaning is first co-created non-verbally in shared projects of discovery, before words or language develop (Condon 1975b, Delafield-Butt and Trevarthen 2015, Trevarthen and Delafield-Butt 2013b). Shared embodied intersubjective intelligence remains a foundation for social understanding throughout life, giving individuals in cooperative engagement a 'second person perspective', before rational and abstract 'theories of mind' develop, and the capacities to share these using words (Reddy 2008).

The brain systems that subserve this second person perspective are becoming increasingly clear, and recognized as the ‘mirror neuron’ systems that resonate between individuals to allow a shared understanding of another’s intentions as they are acted out through movements of the body (Rizzolatti and Sinigaglia 2008, Gallese et al. 2009, Schilbach et al. 2013). This presents an embodied social understanding conveyed through movements, which becomes the foundation for the capacity to reflect on this knowledge of the other for a more abstract, rational social understanding. But any cortically-mediated mirror neuron system depends on regulations from sub-cortical motivations that establish fundamental resonances between individuals. These include the brainstem-mediated polyvagal systems of expressive movement responsible for the coordination of gesture, speech, intentional action and – importantly – autonomic visceral activity controlling heart rate, breathing, blood oxygenation and metabolism (Porges and Furman 2011, Porges 2011).

These two systems sustaining vitality, for the individual and consensually, are part of a larger brainstem integration of proprioceptive information across the body into a coherent plan for effective sequences of motor action, which Jaak Panksepp identifies as the ‘primary SELF’ or ‘simple ego-type life form’ (Panksepp 2005, Panksepp and Biven 2012, Panksepp 1998). The acquired capacities of the neocortex to discriminate and remember perceptual information reflectively, and to respond adaptively with refined movements of manipulation or speech, are animated and developed by motives and emotions of this primary Self (Merker 2013, Merker 2007). This fundamental experience of living, perceiving, and acting purposefully in the world appears disrupted in autism.

An embedded hierarchy of conscious purpose, adapted for communication

Nobel laureate Roger Sperry reminds us, “the sole product of brain function is motor coordination” (Sperry 1952, p. 297). Moving purposefully and in communication with each other lies at the heart of what we do, and its form of action is a direct reflection of one’s neurological and psychological integrity. The generation and action plan of movements is informed by a sense of Self-in-Relations with others from the beginning of life, even in the first motor actions of the foetus *in utero* (Delafield-Butt and Gangopadhyay 2013, Trevarthen 2016). At this early age the conscious scope and understanding of actions is limited by lack of experience, but the movements of the foetus are shaped and timed to explore sensations within the body and in the accessible world, and test the contingencies with intention that is sensitive for intimacy with the mother’s expressions of life, or those of a twin. In social interaction with newborn infants, movements of the hands and feet, face and voice, touch and engage another person to communicate the interest and excitement of human life, understood and reciprocated by imitation (Kugiumutzakis and Trevarthen 2015, Trevarthen and Delafield-Butt 2013b).

The individual movements of foetuses or infants are organised in hierarchies of purpose that develop in complexity through infancy and childhood (Figure 1). These begin as simple, single movements to goals, such as the reach of the arm to touch or of the leg to kick, to small projects of serially organised single movements that perform more distal, and more ambitious tasks, such as reach-to-grasp or a reach-grasp-place (Delafield-Butt & Gangopadhyay, 2013). A foetus in the last 10 weeks of gestation makes a movement to suck the thumb with anticipatory opening of the mouth as the hand approaches (Reissland et al. 2014). Such intentional serial organisation of movement arguably shares the same foundation as that of logic (Lashley 1951), giving an embodied motor origin of higher cognition (Pezzulo 2011).

As development proceeds, small projects as are seen in the newborn are themselves serially organised to perform skilled tasks with more abstract goals and distal reach, such as putting on a shoe to go outdoors, dressing for dinner, or cooking dinner before guests arrive. This final, tertiary level of abstract processing is free of the contingencies of the present movement, achieving higher order imaginary ambitions to act, rather than primary process intentions-in-action with prospects of immediate satisfaction. Higher-order abstractions involve what is called ‘mentalising’, and a rational understanding of what has happened in the world that is familiar, and what is likely to happen in the future (Delafield-Butt and Trevarthen 2013, Delafield-Butt and Gangopadhyay 2013).

The tertiary processes are cortically-mediated, whereas the primary and secondary processes evident at birth are brainstem- and limbic-mediated ones (Figure 2)(Solms and Panksepp 2012, Trevarthen and Delafield-Butt 2016). And it is here, in the brainstem at the site of primary process consciousness, that we find signs of the motor deficit in autism with evidence of significant neurological disruptions (Trevarthen 2000, Trevarthen et al. 1998, Rodier and Arndt 2005, Welsh, Ahn, and Placantonakis 2005, Trevarthen and Delafield-Butt 2013a).

These primary process conscious acts are the buildings blocks on which social understanding is made meaningful in life stories (Bruner 1990, 2003, Delafield-Butt and Trevarthen 2013, Trevarthen and Delafield-Butt 2013b). Brought to life in shared, serially organised projects with another person, either directly in face-to-face intersubjective engagement or in shared attention to an object or task, these motor projects form the foundation for experience of narratives that unfolds over time rich with personal meaning and delivering insight into the values of a culture (Delafield-Butt and Trevarthen 2015; Delafield-Butt and Adie 2016). The origins of primary intersubjective narratives between an infant and a caring other are dependent on the precise timing and rhythms of two motor systems operating in time and in tune with one another, generating a 'communicative musicality' in mutual acts of imagination with poetic rhythm and tone (Malloch 1999, Malloch and Trevarthen 2009, Daniel and Trevarthen 2017). And it is this sensory-motor timing with interpersonal awareness that appears to be fundamentally disrupted in autism, preventing social understanding, shared narrative meaning-making, and natural growth in the rhythms and patterns of a family culture (St Claire, Danon-Boileau, and Trevarthen 2007, Trevarthen and Delafield-Butt 2013a). Children with autism do not perceive the vitality inherent in the subsecond timing and form of action – its vitality dynamic – as other children do (Rochat et al. 2013).

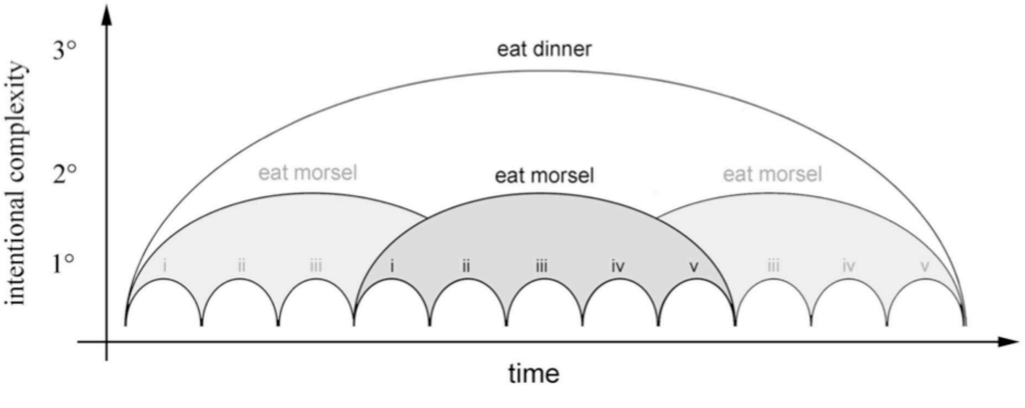

Figure 1. A developmental hierarchy of intentional action. The schematic of the nested organisation of three levels of complexity of sensorimotor intentionality: (1) a primary sensorimotor intentionality operative in individual action units and evident in early fetal life; (2) a higher-order, secondary sensorimotor intentionality that structures and coordinates the primary

actions into small projects with a common goal, evident in late fetal life; and (3) a tertiary intentionality that organises the ones below it, emerging in late infancy and toddlerhood and elaborated throughout human life. In the example illustrated, the distal tertiary intention to ‘eat dinner’ is enacted by a sequence of repeated secondary levels of sensorimotor intentionality, each ‘eat morsel’ itself composed of a sequence of more proximal actions. The primary level is the action units themselves, sequentially ordered here (i) moving the arm to the food, (ii) grasping the food, (iii) moving the food to the mouth, (iv) releasing the food into the mouth, and finally, one link to represent (v) mastication and swallowing. The overlapped primary and secondary levels represent simultaneous activity. In autism, the primary level of action organisation is disrupted in early development, which transmits disorder up the levels to affect motor projects (reach-to-grasp-to-place) and also the integration and coherence of higher order purpose and understanding. Each level of motor organisation matches its counterpart levels of conscious process described in Figure 2 See also Delafield-Butt & Gangopadhyay (2013).

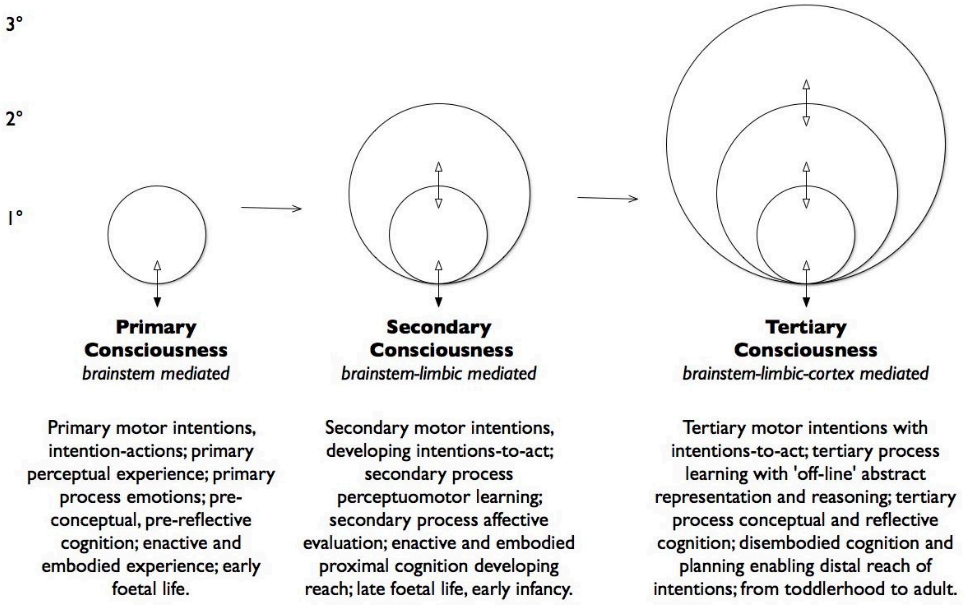

Figure 2. Development of human consciousness. Primary conscious function evident in early foetal life later structures secondary process limbic function as these mature in late foetogenesis. Secondary processes in turn regulate primary processes. As development proceeds and neocortical function comes to the foreground in late infancy and early childhood, these exert control over the activity of secondary process emotions and intentions. A nested hierarchy of top-down and bottom-up regulation ensures coherence across the system, each level conscious and fully functional, contributing to an integrated concious experience in the present moment. In autism, disturbance to primary consciousness disrupts development of secondary and tertiary consciousness. Arrows represent bottom-up and top-down information flow. Filled arrow heads represent engagement with the external world. Expansion of knowledge and affective and perceptual discrimination through learning, reflection, and reasoning made in active engagement with the world, both with social others and in the world of concrete and abstract objects is remembered and expands the content of tertiary consciousness from early childhood throughout life. The capacity of tertiary knowledge to increase enables a rich, projected future of imagined possibilities that come to dominate adult consciousness, and can leave the seconary and primary levels neglected in rational discourse. See also Trevarthen & Delafield-Butt (2016).

LOCATING MOTOR-AFFECTIVE INTELLIGENCE IN THE INTEGRATIVE WORK OF THE BRAINSTEM

The central role of timing and serial ordering in intelligent moving

Analysis of the literature on autism motor deficits identifies three types of error evident in individuals with autism, each affecting *prospective motor timing and integration*

(Trevarthen and Delafield-Butt 2013a): (1) Generation of *single actions*, such as when extending the hand to touch, or indicate, an object of interest; (2) organization of a *series of actions* to perform more complex tasks or projects, including speaking; and (3) simultaneous *coordination of multiple action units* across the body to achieve coherent purpose, as in postural accommodations when standing, walking or running.

To perform a movement well, the timing of every part must be made in precise coordination with all of the muscle state of the rest of the body, balancing all forces of inertia and momentum in synchrony so that the actions give spatial and temporal coherence of purpose to the task in hand (Bernstein 1967, Lee, Craig, and Grealy 1999). Coordination of movement throughout the body, with autonomic integration of regulators of internal vital state or 'energy', is the function of the central nervous system. This integrative action (Sherrington 1906) is generated and regulated first within the brainstem and hypothalamus, working tightly with time-keeping of the cerebellum. Secondarily more precise assimilation of environmental affordances is afforded with the adaptable circuits of the midbrain limbic system and both limbic cortex and neocortex of the forebrain.

Coghill (1929), in his comparative analysis of the animal nervous system, called the brainstem the 'head ganglion of the nervous system', recognizing that it is the primary integrative region of information from the senses and across the body. This information is organised along three principle perceptual axes: (1) *visceroception* of information from inside the body detailing it's vital physiological needs; (2) *proprioception* of the body-in-motion, giving the physical dynamic state of forces in the body as it moves through the world; and (3) *exteroception* from the distance receptors (eyes, ears, nose) and by touch receptors that put the active body and its vital needs within an external environment of people, places, and things (Sherrington, 1906).

Each movement must be prospectively controlled (von Hofsten 2007, von Hofsten 2004, 1993, Lee 2009, 2005). To achieve their purpose, the outwardly directed forces of muscle action must be coupled with compensatory forces in the body to produce a smooth and efficient action, working synergistically with all the other movements across the body. This basic prospective knowledge of the proprioceptive and biomechanical consequences of a conceived action or intention forms the first essential intelligence on which a comprehensive and expanding consciousness of the effects of different actions in different circumstances can be built by learning. As development proceeds, knowledge of the contingencies of the world form a rich conceptual understanding built on the basic template of action-and-response.

The whole 'action-response' system was identified by James Mark Baldwin as a set of ‘circular reactions’ (Baldwin 1895). This theory of generative, agent-led learning stands in contrast to the passive 'stimulus-response' paradigm of the laboratory experiment. The two paradigms address the same fundamental mechanism of learning -- correlation of information between different occasions of life activity. However, the method of testing hypotheses about the mechanism of consciousness and its adaptation isolates the intelligence of a stationary subject in a set world, free of ‘distractions’. In normal circumstances, the human animal self-generates and selects sensory stimulation for its own, vital needs within a ‘speculative’ reality, and in collaboration with other individuals whose manifestations of intentions and feelings are perceived as co-regulators for engagement (Reddy, 2008). Rarely is the animal passive and responsive, as experimental psychology requires for its tests. It is an active generator of the perceptual and affective experiences that make up what Jacob von Uexküll defined as its Umwelt, or the 'life-world' it is 'interested in' (von Uexküll 1957, 1926). It's intelligence is constructed by it and shared by gesture and sign with others intelligences (Sebeok 1977).

A brainstem neurophysiological system for motor control, and communication of motives

The brainstem systems responsible for integration of the sensory and motor information required to perform a simple purposeful act of avoidance, orientation or capture are now recognised to generate a basic psychological experience, called 'primary process functions' (Panksepp and Biven 2012, Panksepp and Northoff 2009). Core feelings, senses of value, and intentions to act in movement are common to all mammals (Panksepp 2011). They are pre-conceptual and pre-reflective, but they are nonetheless fundamentally conscious, generating experiences of awareness that shape learning, and that influence the development of 'higher' midbrain and cortical functional anatomy (Merker 2013, Merker 2007, Vandekerckhove and Panksepp 2011). All lines of evidence – neuroanatomical, behavioural, and psychological – indicate that this core process of action with awareness and affective appraisal is disrupted in autism, and from early in development.

The brainstem takes up information from the senses of proprioception, hearing, touch and taste that are needed for self-regulation of movements, and their use in communication. It responds to music and is a primary site for coordination of movements that engage with the rhythms and affective qualities of melody (Damásio 2010, Porges 2010). Individuals with autism have sensory problems affecting this intuitive awareness. The brainstem includes the autonomic nervous system, which controls levels of arousal and involuntary bodily functions such as breathing and heart rate, and also regulates sleep, all of which can be irregular in people with autism (Richdale and Schreck , Levine et al. 2012, Goodwin et al. 2006).

Brainstem anatomy and functions transform as the body becomes active in new ways in early childhood. Further changes in the volume of the brain stem and cerebellum between 8 and 16 years (Jou et al. 2013, Jou et al. 2009) suggest that in adolescence motor-affective changes associated with ASD will be evident in new ways.

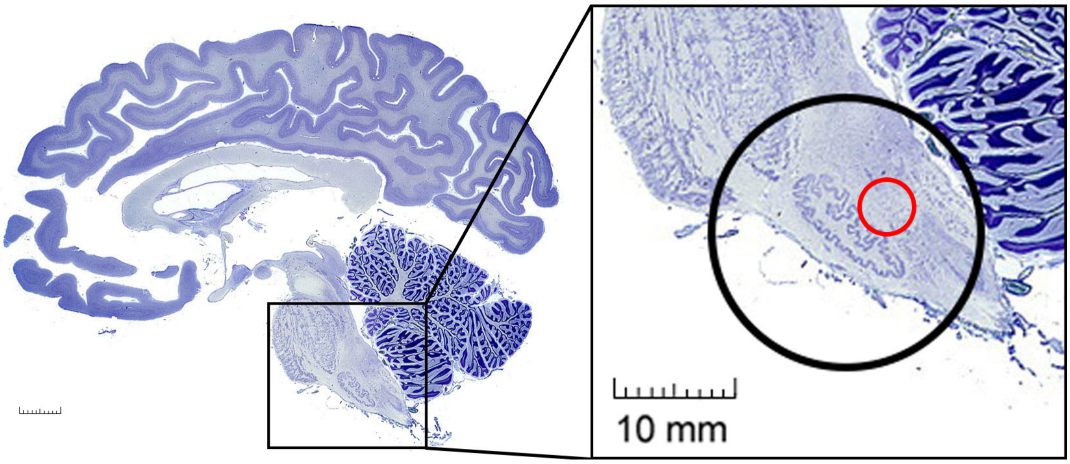

Figure 3. Parasagittal section of whole brain (left side) showing the significant structure of the inferior olivary nucleus with its gyrated layer of cell bodies (right side, circled black) and adjacent nucleus ambiguus (right side, circled red). Adapted with permission from http://www.brains.rad.msu.edu, and http://brainmuseum.org, supported by the US National Science Foundation.

Neurological evidence of brainstem abnormality affecting motor timing in autism: the inferior olive

Early post-mortem histological studies indicated significant structural and morphological differences in brainstem nuclei of individuals with autism (Welsh, Ahn, and Placantonakis 2005). Further, MRI scans of individuals with autism, although unable to resolve the individual nuclei, show consistent change in the overall size of the brainstem in individuals with autism (Jou et al. 2013, Jou et al. 2009). A recent meta-analysis of one thousand brain scans performed across eighteen sites in Europe and North America shows that changes of brainstem volume are one of two significant differences across autistic brains compared to those developing normally (Haar et al. 2014). The other is a change in cortical thickness of the left superior temporal gyrus responsible for movements of speech, and for discriminating awareness of social expressions. These changes in the cortex will have developed as consequences of earlier changes in brainstem systems. In their comprehensive analysis of brain and behaviour, Rodier and Arndt (Rodier and Arndt 2005) conclude, "there is no region but the brain stem for which so many lines of evidence indicate a role in autism" (p. 146).

Arndt et al's (2005) report of brain-region-specific alterations of the trajectories of neuronal volume growth throughout the lifespan in autism suggest cell-cell communication, adhesion, or migration factors in embryogenesis may be affected, and supports the conclusion that the neuroanatomy of the brainstem has been altered prior to birth in people with autism (Figure 3). Further, Bailey at al (1998) report dysplastic configuration of the lamella of a central pacemaker organ, the *inferior olive,* and the presence of ectopic neurons lateral to the inferior olive. Efficient inferior olive function is necessary for the subsecond timing and integration required for efficient, skilled action (Welsh et al. 1995, Llinás 2001). Anatomical disruption to the inferior olive is known to lead to a corresponding functional disruption in sensorimotor timing and integration, due to its particular, tight structure-function relation, a product of dense nuclear packing and shared bioelectric field across cells that affect their combined electrophysiological properties (Welsh, Ahn, and Placantonakis 2005).

An anatomical growth error in the inferior olive appears to explain errors in sensorimotor timing and integration, which arise prenatally and that will cause inefficiency of movement after birth. Inefficiency in early movement, leads to distress and frustration in simple motor tasks and in communication, and an increasing compensatory cognitive load as development proceeds. "Abnormal patterns of motor learning in children with autism spectrum disorder, showing an increased sensitivity to proprioceptive error and a decreased sensitivity to visual error, may be associated with abnormalities in the cerebellum" (Marko et al. 2015) to which the inferior olive directly serves as the principle pacemaker. Subsecond motor timing and integration of skilled movement expands with the development of new cerebellar regulations for fast manual and oral movements that are essential for efficient communication of knowledge and skills in hominids (Hoffman and Falk 2012). We conclude that a growth error in inferior olive morphogenesis will disturb timing and integration of intentions and lead to frustration, social withdrawal, and subsequent cognitive processes of compensation identified as autistic (Delafield-Butt and Gangopadhyay 2013, Trevarthen and Delafield-Butt 2013a, Welsh, Ahn, and Placantonakis 2005).

The inferior olive is responsible for high speed sensory and motor integration with rhythms in the range of 7-13Hz, or one pulse every 150 to 50 milliseconds, which corresponds to the upper limit of consciously regulated rhythmic movements, as in eye saccades, fast finger tapping and rapid speech (Welsh et al. 1995, Osborne 2009, Trevarthen 2016, Delafield-Butt and Trevarthen 2015). Abnormal morphogenesis in early development will lead to mis-timed integration of muscle contractions across the body and distortion of the kinematics of every fast movement, as reported for persons with autism. In consequence the actor's comprehension of intended goals and motor timing to achieve them will be complicated (Whyatt and Craig 2013b, Whyatt and Craig 2013a, Whyatt and Craig 2012, Torres et al. 2016, Torres et al. 2013), as well as how the units of movement are chained together in complex projects and synchronized messages of communication (Fabbri-Destro et al. 2009, Boria et al. 2009, Cattaneo et al. 2007).

Interestingly, kinematic data from a 3-D motion tracking study of simple horizontal sinusoidal (back and forth) right arm movements (Cook, Blakemore, and Press 2013) reveal those movements of individuals with autism to be fast and jerky – lacking efficient regulation of acceleration and velocity and showing an increase in amplitude of the jerk (rate of change of acceleration) as they swung their arms back and forth. Strikingly, the reported increase in jerk amplitude occurred at a rate of 12 Hz, indicative of disturbed inferior olive function (Welsh, Ahn, and Placantonakis 2005). The autistic subjects were also unable to discriminate differences between representations of normal and abnormal movement displays as well as normal subjects. It was concluded that for subjects with autism, "developmental experience of their own atypical kinematic profiles may lead to disrupted perception of others' actions." (Cook, Blakemore, and Press 2013, p. 2816).

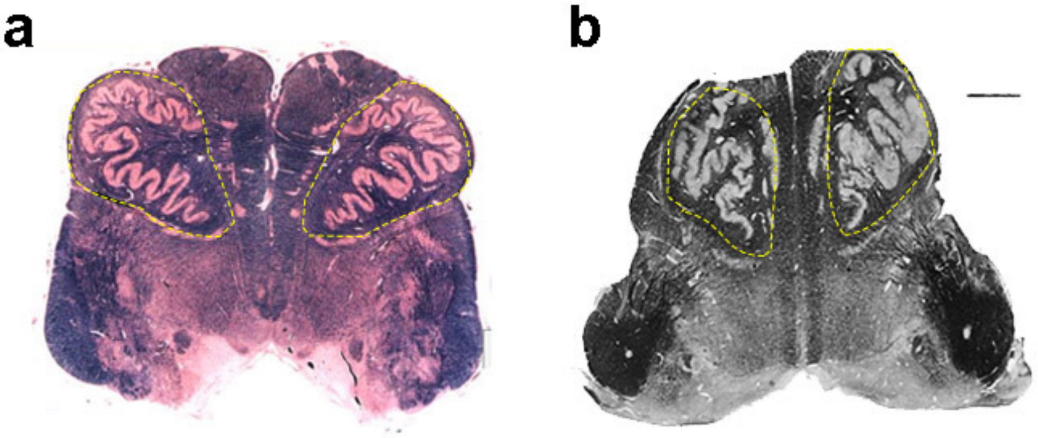

Figure 3. Transverse section through the medulla oblongata showing the dense gyrations of the inferior olive (dotted yellow) in (a) a neurotypical individual and (b) an individual with autism. Note the regular, unbroken, cell-dense gyrations of the inferior olive in (a), but in (b) the inferior olives show an abnormal outline; the band of neurons is irregular and broken up, indicating failure of the neurophysiological coherence for fast, skilled movement timing and integration. This particular individual suffered from severe autism with notable disruption to motor control (see case report reproduced in the appendix). (Luxol fast blue and cresyl violet; bar represents 2.5 mm; reproduced from (Bailey et al. 1998) by permission of Oxford University Press.

A brainstem centre for regulation of social and emotional expressions: the nucleus ambiguus and related systems

Close to the inferior olive is the nucleus ambiguus, of particular interest because of its role in regulation of arousal and expressive movements in social engagement. The Ambiguus is nucleus of origin of motor fibres of glossopharyngeal, vagus, and cerebral portion of spinal accessory nerve, important in the control of speech, vagal regulation of arousal, and transmission to higher cortical regions. It is intimately connected and forms a part of the 'social engagement system'. A growth error in this nucleus would appear to offer an explanation for the flat tone of vocal expression and reluctance to engage in expressive talk, which is a characteristic of children or adults with ASD, although studies investigating disruption of development in the ambiguus are lacking. Variation in vital state mediated by the nucleus ambiguus as part of the polyvagal system, that governs output from the brainstem to the viscera, provide a neuromotor and neurophysiological substratum for 'primary-process instinctual emotions' (Panksepp and Biven 2012, Porges and Furman 2011).

The core integrative pathways of the autonomic or visceral brain have been elaborated through evolution to give an instinctive evaluative foundation for formulating ambitious engagements with a world sensed through movement. They are essential regulators of the development of the most highly developed organs of conscious animal life, culminating in the culture-creating human mind. Secondary-process and tertiary-process emotions expand the capacity of the neocortex to learn. Their emotional evaluations, and representations in thoughts influence free will and intentions to act (Panksepp and Biven, 2012; Solms and Panksepp, 2012). They become confused and weakened in emotional illness, including ASD, requiring therapy that supports regulation of life and its habits by constructive emotions (Panksepp and Biven, 2012).

We find clear evidence that the inferior olive and the nucleus ambiguus, which together mediate motor timing and integration of the polyvagal systems to sustain vital state, enables simultaneous social co-regulations of embodied agency and autopoesis that begins to be active early in prenatal development, before the neocortex is functional in recording refined skills of action and awareness of a world to be richly discovered. Before birth the foetus develops a cooperative ‘amphoteronomic’ sharing of vital resources with the mother. After birth a developing neocortex and cerebellum record mastery of refined skills of action and awareness of a world to be richly discovered with new sensory powers, as the infant and toddler participates in actions and experiences ‘synrhythmically’ with affectionate companions before accepting tools and disciplined practices of a defined culture (Trevarthen et al. 2006). Every step in this growth of understanding adaptation to any abnormality of initiative and awareness is critical in the developing individuals, children and adults.

Additional evidence that brainstem disruption in ASD also affects arousal and social engagement: the locus coeruleus and related systems

In agreement with Welsh (2005), we identify the inferior olive as a likely primary source of disruption of the mind in early prenatal stages by affecting subsecond timing and integration of motor impulses. We propose that information on development of this system and the neighbouring brainstem nuclei that participate in developing emotions, including the nucleus ambiguus responsible for control of expressions for social engagement, will advance our understanding of ASD pathogenesis, and advise how best to respond to it. Moreover, two other tightly related brainstems systems are thought to be affected in autism: those for regulation of arousal to conscious activity, and sensory-motor organs of expression for social signalling.

The 'arousal crescent', extending from the lower brainstem to the hypothalamus, is sensitive to multimodal information and becomes excited by "unpredictability and uncertainty” (Pfaff 2006, p. 55). This basic perceptual and affective discrimination forms a core feature in the identification and thus use of information from experience—facilitating the generation of a sense of meaning of a stimulus set within its environment, producing generalized brain states. The *locus coeruleus*, a group of cells at the lower brainstem of all mammalian animals, responds to sudden, salient information important for contextualising it's meaning in terms of heightening arousal. Heightened sensitivity to multimodal sensory stimuli and inappropriate or de-contextualised responses are regular features of autism (Donnellan, Hill, and Leary 2013, Kushki et al. 2013). These inappropriate responses will have a profound effect on the ability of individuals with ASD to formulate generalisable brain states, creating strain and may lead to co-called 'weaken central coherence' with compensatory attention to local detail and repetitive movement(Happé and Frith 2006).

The polyvagal social engagement system identified by Porges (2011), with its lynchpin centred on the nucleus ambiguus, is an emotional expressive system mediating insight into feelings within another's experience and intentions. Uniquely developed in humans and social mammals (Porges 1995, 2001, Porges 2007, Porges and Furman 2011), this system provides the foundation for a body language of signs that refer to objects and their practical uses. The system also provides direct neurophysiological coupling between autonomic self-regulation of visceral state and social cooperation, by communication via facial expression, voice, and manual gesture. Evolutionary adaptation in vagal regulation of the autonomic nervous system together with the evolutionary emergence of an integrated social signalling system enables complex visceral regulations of self-awareness or 'being alive' to be shared socially:

"… phylogenetic transitions resulted in brainstem areas regulating the vagus becoming intertwined with the areas regulating the striated muscles of the face and head. The result of this transition was a dynamic social engagement system with social communication features (e.g., facial expression, head movements, vocalizations, and listening) interacting with visceral state regulation." (Porges 2011, pp. 203)

Abnormal excitability or indifference to threatening stimuli, combined with flattening or narrowing of expressive behaviours in communication may explain symptoms identified with autism in childhood. Specifically, these will affect the way in which a child cooperates and shares feelings with family and teachers, requiring special sensibility in response.

INTRINSIC AND ENVIRONMENTAL FACTORS AFFECTING ASD THROUGH THE COURSE OF DEVELOPMENT.

The cause of these growth errors that we have identified as the initial cause of ASD are likely any combination of genetic (Aitken 2010), environmental (viral or stress-related), or naturally occurring spontaneous errors of epigenetic regulation. A considerable portion of the genes that have been implicated in autism pathogenesis are found to be expressed in the brainstem (Nolan, personal communication). Yet, the story is complex. ASD pathogenesis results from some significant interaction between genetic and environmental factors, with genetic factors accounting for less than half of its aetiology, demonstrating the environment, including the social environment, is a significant factor (Hallmayer et al. 2011, Sandin et al. 2014).

It is important, for both understanding of the atypical behaviours of young children with ASD, and for provision of beneficial treatment or therapy, to recognize that the response of other persons, especially parents in early years, may contribute to their difficulties in self-regulation and in communication and learning. There is evidence from videos of interactions between a parent and an infant who is later diagnosed with autism, that the disordered attention, reduced expressive behaviour and play, and repetitive motor activities recognized by parents as deviant (Saint-Georges et al. 2010) lead them or other carers to use exciting, distracting, controlling or restraining behaviours, which confuse the child (St Claire, Danon-Boileau, and Trevarthen 2007). In their affectionate efforts to help the child, caregivers may contribute to the child's difficulties. This problem may be assisted by professional advice that demonstrates to the caregivers how the child responds better with less persuasive attentions.

CONCLUSIONS: IDENTIFYING AND SUPPORTING PROBLEMS ARISING FROM DISRUPTION OF MOTIVES FOR DEVELOPMENT OF COGNITION AND INTERPERSONAL RELATIONS

Once one accepts that the organisation, control, and structure of human movement is fundamental for our intelligent behaviour as the primate with most advanced motor intelligence (Graziano, 2009), not only in single acts to reach identified goals using experience of objects that excite interest in the present moment, but for mental composition of imaginative purposes and the coherence of complex projects that develop through a lifetime of learning cultural habits (Donaldson, 1992), then the role of the motor deficit identified in autism pathogenesis becomes clear. Levels of cooperative awareness and the sharing of cultural meaning depend on affective and cooperative social engagement of imaginative movement. Children with autism find it difficult to sustain more complex purposes in activity, with sure appreciation of what the environment affords now and what the future may hold. They are also confused by instruction, especially if it is imperative and unreceptive, which leads them to ‘fall behind’ in the attainment of ‘common sense’.

Research shows that the degree of motor skill and coordination in young children is correlated with their academic skill and attainment in school. There is a tight link between the development of movement in early childhood and the development of intelligence (Davis, Pitchford, and Limback 2011, Pagani and Messier 2012, Wassenberg et al. 2005), as the neurologist and pioneer therapist Geoffrey Waldon discovered (Solomon, Holland, and Middleton 2012). Response to this developmental process requires adaptation of methods of assessment and education to appreciate basic motor processes of intention and communication (Teitelbaum and Teitelbaum 2008, Teitelbaum et al. 1998, Delafield-Butt and Gangopadhyay 2013, Trevarthen and Delafield-Butt 2013a, Acquarone 2007).

We propose that appreciation of difficulties from the point of view of a child with autism, with deliberate attention to their initiatives, is essential for optimal education and emotional support in companionship. Comprehending their feelings and awareness is made easier by a theory of learning that recognizes evidence that the human brain grows with regulations from brainstem functions that determine how knowledge and skills are acquired by activation and modification of forebrain cortical functions – regulations that are made apparent in pre-rational expressive movements from prenatal stages. Research on the foundations of motor intelligence, that links studies of brainstem systems and the cerebellum with intra-uterine studies of the maturation of movements in the fetes, is particularly promising.

Methods of therapy and education that support hopes for movement

Experienced therapists trained to attend to, and wait for, small positive initiatives of the child for progressive and enjoyable interaction can strengthen communication and shared enjoyment as well as benefitting confident states of self-regulation and fluency of movement (Amos 2013). In a remarkable study, parents assisted to engage with sensitive attunement to the feelings and intentions of their child with autism significantly improved their child's long-term socioemotional well-being and reduced symptom severity (Pickles *et al* 2016). Sensitive psychoanalytically informed methods practiced for early intervention, and 'art' therapies that support willing engagement in song, musical performance or dance have been shown to be helpful both for affected infants and toddlers and for their parents (Acquarone 2007). In the introduction to the second edition of his book *The Interpersonal World of the Infant*, which sought to focus the attention of psychoanalysts on non-verbal narratives of feelings and affect-loaded memories or habits, Daniel Stern appreciated the strong response his account of 'the interpersonal world of the infant' received from practitioners of dance, music, body, and movement and existential psychotherapies (Stern 2000, p. xv). His book on Vitality Dynamics (Stern 2010) pursued and greatly enriched this approach, which certainly has an application for individuals with ASD of all ages. Indeed, there are a great variety of methods aimed to support acting, thinking and communication for cooperation in children with autism; for example, with encouragement to play (Daniel 2008; Daniel and Trevarthen, 2017), to respond to being imitated (Nadel 2014), or to participate in a form of dance movement therapy (Trevarthen and Fresquez 2015).

Questions at the forefront of understanding how the brain for purposeful movement develops, and how it learns

We now need improved knowledge of key components of the primary motor/affective systems in the brain, including the form and function of the inferior olive and associate nuclei such as the ambiguus using high resolution brain scanning techniques, or focussed post-mortem histological assessment. In the case of the former, preliminary data demonstrate 7T MRI can delineate the inferior olive brainstem nuclei with some precision, offering a precise technique for imaging the brainstem that was previously unavailable. Moreover, the neurological abnormalities discovered can be related to motor kinematic measures. On the other hand, post-mortem histology offers the advantage of cellular, and genetic resolution for detail at the molecular level of brainstem composition. Both routes offer promising and insightful new information into the aetiology of autism.

Further, motor kinematic studies will benefit from this detailed account of the source of inefficiencies in a movement, whether measured as units of acceleration and deceleration in spontaneous movement (Whyatt and Craig 2012, Crippa et al. 2015) or as the jerk profile (Cook, Blakemore, and Press 2013). Disruption to the inferior olive predicts the change in regulation of these characteristic features of motor inefficiency, yet this link has yet to be fully explored.

Finally, as the field as a whole comes to understand and characterise the particular motor deficit in autism, so we will begin to define its motor signature (Anzulewicz, Sobota, and

Delafield-But, 2016). Clarification of an autism-specific motor signature, with its affective regulations, will help to identify novel, non-invasive bio-behavioural markers for autism and give resolution to specific neurological changes in autism in the brainstem responsible for generating the feelings and intentions of the primary self expressed and formed through movement. Attention to these motor changes provides an exciting new route to improved practice for therapists and families that attend to the primary nature of the individual as embodied, emotional, intentional, and not necessarily verbal. The brainstem-mediated primary self is ontogenetically prior to, and generative of, a reflective, conceptual self made richly communicative in language.

This primary self remains fundamental for social connection and meaning-making, and for attention in mental health and well-being. But its basic nature can be lost in our social world with its technical demands of prescribed behaviours and appropriate language.

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Appendix

Case History of Case 1 (reproduced from Bailey et al. 1998).

Aspects that involve movement are highlighted in *italics* (authors own) to draw attention to the prevalence of movement and its putative underlying motor disruption in each act:

> As a baby he was a poor feeder who disliked being held. A clinical hearing test was failed at 7.5 months but the parents knew that he could hear soft sounds and was sensitive to vibrations. He had *persistent difficulties with gross motor control*, *was clumsy* and did not chew. He could be propped to stand at 2 years

of age but *could not move from this position*. He acquired *a few sounds but no speech*; he screamed frequently, especially if there was an echo. He did not turn to his name or speech, and never followed eye gaze or pointing. He could sometimes follow simple instructions, particularly if context bound. He did not imitate or copy, but would sometimes point to a picture in a book. In infancy he continued to dislike being held and sometimes urinated when picked up. He took no interest in people and would only look at his parents if they jumped and waved their arms. He appeared to focus on parts of people and was more interested in his parents' glasses and earrings than their faces; he was particularly interested in buckles and zips. He could spot small items such as milk bottle tops and paper clips but would ignore large objects in the environment. He would not seek comfort if hurt. He would *bite* his parents and other children, and appeared to enjoy the chaotic reaction that this provoked. He became increasingly destructive and overactive. He was interested in mechanical things and would spend most of the day in minute examination and manipulation of tiny objects; *his fine motor co- ordination appeared unimpaired, although he acquired few fine motor skills*. He liked to fiddle with bunches of keys, and would attempt to put these in locks. He enjoyed watching a spinning top, and would spin wheels for hours; he also liked watching credits at the end of television programmes. He *flicked light switches repeatedly*. He would often *flap his arms and pant*, particularly if excited, and this could be *accompanied by rocking on his toes*. He liked to look at the ceiling and *spin*, and also enjoyed going on roundabouts. *In the 1st year he rubbed his feet together and clenched his hands together in the midline; when older he engaged in hand stereotypies* *close to his face. He gnawed at his fingers and nails, head-banged and pulled at his penis.* He appeared intrigued by pain; he went back repeatedly to an exposed mains socket to get a shock and he cut himself with a razor. He would occasionally cry if he hurt himself but appeared insensitive to temperature. He had marked pica and would drink the water in a paddling pool until sick.