*Masters of Research (MRES 2014)*

*Supervisor: Dr Jon Brock*

*Student number: 43537227*

*Date of submission: 04/10/2014*

# ANTICIPATORY POSTURAL ADJUSTMENTS IN AUTISM

Beverley Witherington

Macquarie University Department of Cognitive Science

## *Table of Contents*

**RESEARCH SUMMARY** ..... 3

**CHAPTER 1– LITERATURE REVIEW**

1.1 – INTRODUCTION ..... 4
1.2 – LITERATURE SEARCH ..... 6
1.3 – AN OVERVIEW OF AUTISM
*1.3.1 – Autism diagnosis and prevalence* ..... *7*
*1.3.2 –Symptomology in autism* ..... *8*
*1.3.3 – Autism and cormorbidity* ..... *10*
1.4 – AETIOLOGY AND AUTISM ..... 12
*1.4.1 – Genetics of autism* ..... *13*
*1.4.2 – Neurobiological research in autism* ..... *14*
*1.4.3 – Cognitive neuroscience theories in autism* ..... *16*
1.5 –NEUROMOTOR FUNCTION IN AUTISM
*1.5.1 – Processes of motor control* ..... *18*
*1.5.2- Developmental profile of motor symptomology in autism* ..... *21*
*1.5.3 - Perceptual motor processes* ..... *23*
*1.5.4 – Praxis and imitation* ..... *25*
*1.5.5 – Motor coordination and bimanual coordination* ..... *28*
*1.5.6 –Postural control* ..... *30*
*1.5.7 – Neurophysiological basis of motor symptomology in autism* ..... *34*
1.6 - DISCUSSION ..... *39*

**CHAPTER 2 – RESEARCH DESIGN**

**ABSTRACT** ..... 41

2.1 - INTRODUCTION ..... 42
2.2 - METHODOLOGY ..... 49
2.3 – RESULTS ..... 54
*2.3.1 Purdue Pegboard Test* ..... *54*
*2.3.2 EMG Data* ..... *55*
2.4 - DISCUSSION ..... *60*

**BIBLIOGRAPHY** ..... *67*

## *Research Summary*

Accuracy in coordinated movement depends on postural control, and also anticipatory behaviour, which enables the individual to predict the outcomes of planned motor action, and thus contributes to the precision in human movement performance. This anticipatory capacity arises through the generation of anticipatory postural adjustments (APAs) or changes in background muscle activity that precedes volitional movement.

In autism, impairments in anticipatory mechanisms have been reported in recent research, however, to date, APAs have not been examined in adults with autism. The objective of this study is therefore to quantify APAs in adults with autism spectrum disorders (ASD) compared to IQ-matched neurotypical participants to thus advance knowledge of the neural basis of substantiated motor impairments in autism, specifically in relation to movement coordination. This current study involves analysis of APAs generation via surface electromyography (sEMG) of the biceps brachii, within the framework of a bimanual load-lifting task (BMLL), requiring high-level neuromotor coordination and APAs implementation. In contrast to previous studies of APAs in autism, participants in both the autism and neurotypical groups showed similar, efficient anticipatory postural adjustments to counterbalance the unloading event in the BMLL task therefore suggesting anticipatory mechanisms for predictive motor behaviour is intact in the individuals with autism. These findings thus aid clarification in recent literature concerning anticipatory behaviour in autism.

# *Chapter 1*

## *Literature review*

### *1.1 Introduction*

Autism, a pervasive, neurodevelopmental condition (Happé & Frith, 2014; Ozonoff et al., 2014) is now defined as a spectrum condition in accordance with the latest revision of the Diagnostic and Statistical Manual of Mental Disorders (DSM) (American Psychiatric Association, 2013), the DSM-5. This revision of the DSM-5 thus recognizes the extensive phenotypic heterogeneity that presents in individuals with autism. However, autism is unified diagnostically by the clinical dyad of universal impairments in socio-communicative traits and presentation of repetitive, restricted behavioral patterns and interests (American Psychiatric Association, 2013).

As well as these core diagnostic symptoms in autism, a wide range of concurrent conditions present in a large number of individuals with autism, including medical, developmental and psychiatric conditions, with the second highest percentage of concurrent conditions pertaining to motor abnormalities (≤ 79%) (Lai, Lombardo, & Baron-Cohen, 2014a). Irrespective of the high prevalence of motor disorders in autism, motor symptomology is not included within the diagnostic criteria of the DSM-5.

Furthermore, despite both behavioral and neurological research substantiating an extensive range of motor impairments in autism, (Downey & Rapport, 2012) and motor dysfunction delineated as a preliminary diagnostic marker (Landa, Gross, Stuart &Bauman, 2012; Rinehart & McGinley, 2010) as well as central symptom in ASD (Ben-Sasson et al., 2009; Mari, Castiello, Marks, Marraffa, & Prior, 2003), research in motor function has historically attracted much less attention than the core diagnostic features of autism.

However, the premise of motor impairments as a central feature of ASD has driven research focused upon quantifying motor symptomology in autism and its potential

causations. In particular, a recent meta-analysis which identified 83 ASD studies on posture and motor coordination, determined a large effect size between autistic individuals and typically developing controls, and concluded that coordination deficits across a wide range of behaviors, were a core trait of ASD (Fournier, Hass, Naik, Lodha, & Cauraugh, 2010). Additionally, impairments in postural control were viewed as pervasive throughout the spectrum of autism.

Thus, for both diagnostic and clinical purposes, investigations of impaired coordination and postural mechanisms in ASD may advance the clinical conceptualization of autism. As yet however, there is limited research in adults with autism, that details motor function, including postural mechanisms and its relationship to coordinative function. In particular, no studies to our knowledge have quantified the generation of anticipatory postural adjustments (APAs), integral to postural control, in autistic adults. Thus, on the basis of extensive substantiated motor symptomology in ASD, and the paucity of research concerning postural control and associations with motor coordination, this review aims to examine motor function in ASD, with a particular focus on postural mechanisms and coordination.

Within this review Chapter 1 focuses on aspects concerning the character and causation of autism, followed by an outline on motor symptomology, including core motor impairments in individuals in autism. The research study, presented in Chapter 2 is aimed at quantifying APAs, that function to minimize the consequences of predicted postural perturbations to maintain a state of equilibrium of the body, in adults diagnosed with autism and IQ-matched controls.

### *1.2 Literature search*

The literature search was carried out utilizing Web of knowledge, PubMed, and Psychinfo engines between February 2014 and October 2014. 24 Search terms were used to encompass the wide range of articles concerning autism, anticipatory postural adjustments and coordination, comprising of: autism, ASD, anticipatory postural adjustments, APAs, coordination, bimanual coordination, motor coordination, bimanual load lifting task, internal action models, motor control, motor learning, perceptual-motor, neuromotor, motor skills, imitation, motor planning, motor impairments, postural control, dyspraxia, genetics, neurobiology, comorbidity, heterogeneity and neuroimaging.

Consideration was given to specific and divergent fields to ensure each search produced substantial evidence within the published field of literature. Further analysis of an article was dependent on the existence of the search terms within the body of the article. Exclusion of articles occurred if the articles were not accessible in English. The search strategy and the inclusion criteria led to a total of 136 articles that were incorporated in this review. Throughout the review process, various theories relating to autism, anticipated postural adaptions and bimanual coordination emerged and these articles were systematically categorized and examined within these theories. On the basis of comparable concepts in the body of the available literature reviewed, the following categories emerged: Supplementary motor area (SMA), basal ganglia, corpus callosum, cerebellar role in motor and cognitive function.

## *1.3. An Overview of Autism*

### *1.3.1 Autism diagnosis and prevalence*

In the DSM-5, the umbrella term of autism spectrum disorder (ASD), consisting of a collection of neurodevelopmental conditions, is utilized exclusively, with all current pervasive neurodevelopmental condition subtypes[1] excluding Rett syndrome, encompassed under this one diagnostic category (American Psychiatric Association, 2013). These subtypes however, are distinct at clinical (relating to developmental patterning, or trajectories, and comorbidity), cognitive, and aetiological levels (concerning genetic and environmental correlates) (Lai, Lombardo, & Baron-Cohen, 2014b).

Also required to be integrated within the diagnostic qualifying statements is clarifying features, such as level of cognitive impairment and severity levels (Gabis & Pomeroy, 2014). In addition, the diagnostic criteria has shifted from a triad of symptoms to the aforementioned dyadic description, with atypical language development, despite varying language impairments commonly occurring in individuals diagnosed with autism, being removed from the diagnostic criteria and re-classified as a co-occurring condition (Boucher, 2012).

Of relevance, changes within diagnostic criteria potentially influence the prevalence of autism, which is seen to have steadily risen over the past decade, despite consistent use of the DSM-4 criteria (Coury et al., 2014). Although, increased prevalence may be accounted for by a number of factors, such as, increased risk factors, widening the concept of autism to include varying phenotypes, and greater awareness and recognition, which notably is linked to an earlier age of diagnosis (Parellada et al., 2014). Specifically, the present median global prevalence of ASD is described as 0.62-0.70%, (Elsabbagh et al., 2012), however 1-2% estimates have been shown in recent epidemiological studies (Matilla, Kielinen, Linna et al., 2011).

[1] Autism, Asperger's Syndrome, Pervasive Developmental Disorder not otherwise specified (PDD-NOS) and Childhood Disintegration Disorder

Furthermore in relation to autism prevalence, gender differences exist, with males affected consistently higher than females (ratio 1.33 -16.0 in AD, and 3.3-15.7 in PDD) (Elsabbagh et al., 2012; Jeste & Geschwind, 2014). However, empirical data indicates high functioning females are diagnosed later, hence suggesting a diagnostic bias towards males. This finding nonetheless, may represent a higher compensation or camouflage effect in females (Lenroot & Yeung, 2013). Taken together, these findings outline the importance of evaluating aetiological roles of sex-linked factors at various levels that encompass genetic, epigenetic and environmental domains.

The following discussion presents the variable symptomology in individuals with autism, and outlines a range of characteristics, termed co-morbid conditions that commonly occur in individuals with autism.

### ***1.3.2 Symptomology in Autism***

Considerable variation exists in autism from person to person in relation to symptom expression (Matson & Jang, 2014) severity and range of symptoms, and the presentation of additional traits within physical, biomedical, cognitive and neuropsychiatric dimensions (Gabis & Pomeroy, 2014). This diversity of characteristics across the diagnostic spectrum reflects the extensive heterogeneity in etiological, cognitive and also behavioral domains.

However, core features are shared in individuals with autism, comprising of the impaired social interaction and reciprocity, difficulties in understanding, developing, and sustaining relationships, specifically peer relations (Chevallier, Kohls, Troiani, Brodkin, & Schultz, 2012), delays or deficits in verbal and non-verbal communication, (van Buijsen, Hendriks, Ketelaars, & Verhoeven, 2011 ) and, stereotypic, repetitive interests and activities, and restricted behaviors (Funabiki, Murai, & Toichi, 2012; Kaiser, Delmolino, Tanaka, & Shiffrar, 2010).

In examining early symptomology in autism, the core symptoms identified in ASD emerge in stages of delayed, diminishing, or atypical development within the first 12

months of age (Elsabbagh & Johnson, 2010). Atypicalities or delays often present in reciprocal affective behaviour, joint attention (Ozonoff et al., 2014), visuomotor exploration, imaginative play, responding to own name ( Wilke, Tarbox, Dixon, Kenzer, Bishop &Kakavand, 2012) implicit perspective taking, verbal and non-verbal communication, imitation and motor function (Stewart, McIntosh, & Williams, 2013). Additionally, restricted, repetitive behaviors and interests, inflexible disengagement of visual attention and extreme temperament (Elsabbagh & Johnson, 2010) often occur in early development.

Despite the presentation of early symptomology in autism, children identified with ASD on average, are diagnosed after 4 years of age (Centers for Disease Control and Prevention, 2014). A recent study aimed at developing indicators for early diagnosis in autism, studied over 2000 children (ages 17-37 months) at risk of disability, utilizing the Baby and Infant Screen for Children with autism traits (BISCUIT). Five items critical for early diagnosis were identified using functional analysis and receiver operating characteristic (ROC) analysis. The emergent criteria included "development of social relationships; use of nonverbal communication; engages in repetitive motor movements for no reason; shares enjoyment, interest, or achievement with others; and interest in participating in social games, sports, and activities" (LoVullo & Matson, 2012, p .970).

Beyond early development, late onset characteristics emerge in relation to atypical cognitive profiles, including atypicalities in social perception and cognition (Happé & Frith, 2014) executive function, and perceptual and information processing (Ben-Sasson et al., 2009). Specifically, the features associated with social cognition include atypicalities in social interaction, recognizing facial emotions (Katsyri., Saalasti, Tiippana, Wendt, & Sams, 2008), motion perception, social attention, socio-emotional relating, social motivation (Chevallier et al., 2012), emotional regulation (Bachevalier & Loveland, 2006), mentalizing and visuo-perspective taking (Zwickel, White, Coniston, Senju, & Frith, 2011), self- representation; involving altered psychological aspect of 'self' (Uddin, 2011), and alexithymia; concerning difficulty understanding and describing own emotions and metacognitive awareness ( Lombardo & Baron-Cohen, 2011). The features associated with executive function emerging later in maturation are proposed to be impaired social

interaction, cognitive flexibility, planning, inhibitory control and memory (including semantic and working memory) (Boucher, 2012). In addition, perceptual and information processing features encompass systemizing, central coherence, global vs. local perceptual functioning and sensory stimuli sensitivity (Jasmin et al., 2009).

Lastly, in adolescence and adulthood, individuals with autism experience challenges in various aspects of independence, and also in the development of relationships. Furthermore, neuropsychiatric conditions are frequently reported in the stages of adolescence and adulthood. In particular, in individuals with high functioning autism, a high prevalence in social anxiety disorder has been outlined (Hollocks et al., 2014).

Overall, widespread difficulties in socio-communicative capacities associated with impairments in social cognition, greatly compromise abilities in social adaption, with consequences in navigating the social world. For individuals with autism, this difficulty is enduring, and presents irrespective of levels of intelligence, or language ability.

### *1.3.3 Autism and comorbidity*

The high rate of comorbidity in autism, posited to be greater than 70%, is seen to be associated with a series of factors including shared pathophysiology, secondary effects of developing with autism, shared symptom dimensions and related mechanisms, and also overlapping diagnostic criteria (Lai et al., 2014a). Co-occurring conditions range from medical, developmental, and psychiatric conditions, with onset commonly occurring in childhood, and continuing into adolescent and adult stages (Matson & Jang, 2014).

Common medical comorbidities include epilepsy, which occurs in approximately 40% of autistic children (Gabis & Pomeroy, 2014), however late onset is also seen in adolescence and adulthood (Mannion & Leader, 2013). Further medical conditions include immune dysregulation (Fatemi et al., 2012), gastrointestinal problems (Jeste & Geschwind, 2014), sleep disorders (Klintwall et al., 2011) and genetic syndromes, or syndromic autism, wherein autistic characteristics are a common phenotypic expression in multiple

genetically determined neurodevelopmental conditions, including Fragile X Syndrome, Tuber Sclerosis, Angelman Syndrome and Rett Syndrome (Moss &Howlin, 2009).

Co-occurring neuropsychiatric disorders comprise of obsessions, phobias, anxiety and depression (Gabis & Pomeroy, 2014). Recent studies examining comorbid pathophysiology in infants and children with autism, (ages 17-37 months) in comparison with atypically developing children without ASD and children with Pervasive developmental Disorder-Not otherwise specified (PDD_NOS), reported significantly higher sleeping and feeding problems (Kozlowski, Matson, Belva and Rieske, 2012) as well as higher anxiety and avoidance scores (Davies et al, 2012) in the children with autism. A further study investigating executive function (EF) and social cognition and their relationship to anxiety and depression in autistic adolescents, reported that greater anxiety was associated with poorer EF, though no relationship was shown between higher levels of social cognition and greater levels of anxiety (Hollocks et al., 2014).

Within developmental conditions, subnormal cognitive function is estimated at a rate of approximately 50%, measured at 2 standard deviations below the mean, thus indicating a score of <70 on standardized IQ tests (Gabis & Pomeroy, 2014). Gender in ASD has also been examined in relation to IQ, wherein male: female ratio appears to be largest in individuals within normal IQ levels (Gillberg, Cederlund, Lamberg, Zeijlon, 2006). Also of note, savant skills and higher cognitive function is reported to be prevalent in autism despite cognitive impairments (Johnson &Meyers, 2007). The savant syndrome although largely unexplained, is proposed to be related to both implicit and explicit learning, advanced perceptual processing, spontaneous learning and creative manipulation of the integral structures of complex information systems, such as music, numeracy and visual perspective (Dawson et al., 2008). Taken together, these findings highlight the complex relationship between gender, IQ, and symptomology, thus more comprehensive assessments are required to fully understand cognitive function in ASD (Ryland, Hysing, Posserud, Gillberg, & Lundervold, 2014).

As outlined previously, in the DSM-4 language impairments in autism were a defining trait, though this impairment is now excluded in the DSM-5. A high variability in

language presents among individuals and subgroups, with communication difficulties persisting over time, and irregular communication trajectories frequently occurring. Autistic regression, often occurring at 2 years of age, is strikingly defined within language skills (Matson, Kozlowski, & Matson, 2012), with a regression rate of 30% found in a recent child study (Xi, Zhao, &Lui, 2010) .

Language deficits range from technical speech problems, such as articulation, rhythm, modulation, tone and pitch possibly reflecting structural aspects in respect to brain functioning (Billingsley-Marshall, et al., 2007), to inflexible language, inappropriate turn taking, misunderstanding 'figure of speech', misinterpretation of non-verbal communication, and difficulty utilizing language in the social context. Overall, the qualitative and quantitative symptomology of language delays and impairments in autism represents an ongoing challenge in defining causation, and thus devising interventions to enhance communication skills.

The subsequent discussion concerns the genetic, neurobiological and neurocognitive basis underlying the aforementioned autistic traits, highlighting the importance of research in these areas in the development of a more definitive clinical conception of autism.

### ***1.4 Aetiology and autism***

In investigations of causation, a definitive aetiology of autism remains unknown despite considerable research in autism targeting molecular, neurobiological, circuitry, and neurocognitive factors underpinning the core characteristics in autism. This lack of definitive causation constrains conceptualizing autistic heterogeneity, and importantly, the development of diagnostic criteria and intervention strategies. Advancing research to develop paradigms that encompass neuroimaging, genetics, neurobiology and cognitive science may thus provide insights into the developmental trajectories of autism, and also contribute to efficacious interventions.

### *1.4.1 Genetics of autism*

The perspective of autism as a highly heritable neurodevelopment disorder has been reinforced over the past two decades, due to rapid scientific advances in molecular genetics and neuroscience. Specifically, multivariate genetic analysis of autistic symptoms, suggests a heritability of approximately 80% for socio-communicative impairments, and restricted, repetitive interests and activities (Berg & Geschwind, 2012). Furthermore, heritability in autism is seen to occur within the context of gene-environment interplay and also environmental risk, which are both assumed to be contributory to pathogenesis of ASD (Murdoch & State, 2013). Also of note, low genetic correlations are found for autistic symptoms within the general population, (Ronald, Happe, & Plomin, 2005) indicating symptom presentation by chance (Plomin, DeFries, McClearn, 2008).

In addition to the complexity of heritability in ASD, association, linkage, cytogentics, whole-genome linkage or association and whole genome or exome sequencing has demonstrated the diverse and elaborate architecture of autism (Geschwind, 2011). Thus far, genetic research has identified multiple genetic variants, with a high degree of pleiotropy and also of locus heterogeneity (with up to one thousand genes being implicated) (Eapen, Crnčec, & Walter, 2013), large-effect rare mutations and also small-effect common variants (State & Levitt, 2011).

Additionally, recent developments in genomic technologies, in conjunction with large patient cohorts leading to a substantial pool of established genes and loci, has further contibuted to research in pathology at cellular, molecular and circuitry levels (Murdoch & State, 2013). Within this research, several findings have recently emerged, comprising of; *1).* known monogenic neurodevelopmental syndromes linked to high social disability risk, as well as rare pedigree of Mendelian inheritance ( syndromic autism) ( Morrow, et.al, 2008), *2).* established rare and de novo mutations contributory to population risk, *3).* common polymorphisms which contribute to increased risk, although individual alleles with small effect sizes and underpowered cohorts remain unclear in relation to risk ( Klei,

et.al, 2012), *4).* the involvement of established locus and allelic heterogeniety is striking, though, disorder-related genes are found to indicate a reduced set of biological processes, in which these loci converge, *5).* marked phenotypic variance of ASD mutations,with identical variants linked to diverse individual outcomes aside from ASD, comprising of epilepsy, language imparment, intellecual disability, schizophrenia, and typical development, and *6).* marked overlap between syndromic ASD and idiopathic autism (Murdoch & State, 2013).

Overall, the diversity of genetic architecture of ASD highlights the importance of evaluating associations between specific gene variants, brain functions and behavioural ability, and syndromes of known genetic caustation, as well as developing comparisons to neurotypical populations. Research within this vein, may provide insights into developmental genetics in autism, and contribute to understanding the variability in developmental trajectories in individuals with autism (Johnson and deHann, 2011).

### ***1.4.2 Neurobiological research in autism***

In examining the neurobiological basis of autism, emergent evidence demonstrates atypical neuroanatomical, molecular and cellular mechanisms, in addition to altered network activity, rather than dysfunction within specific brain regions (Parellada et al., 2014). However conflicting findings in research concerning neurobiological processes in autism persists, thus constraining advances in this domain. Also, the heterogeneous nature of ASD acts to further limit neurobiological studies.

Specifically, the neuroanatomical features in autism comprise of an atypical acceleration of brain growth within 24 months of age (Raznahan et al., 2013). Specifically, research in autistic children analyzing head circumference and brain volumes has indicated brain enlargement to be a more consistent finding (Wolf, 2013). Later in childhood, amygdala enlargement has been reported (Nordahl, Scholz, Yang, et al., 2012) and increased brain volume in boys has been evidenced via neuroimaging (Herbert, Harris, Adrien, Ziegler, Makris & Kennedy, 2002).

Further in ontogeny, neural systems presenting with atypicalities in the mature brain in autism, include the following; fronto-thalamic-striatal system, fronto-cerebellar network, and fronto-temporal circuitry (Lombardo, Chakrabarti, Bullmore, & Baron-Cohen, 2011). In addition, reduced corpus collosum volume (Frazier & Hardan, 2009) and increased cerebellar hemisphere volume (Stanfield, McIntosh, Spencer, Phillip & Lawrie, 2008) has been outlined in later maturation. Notably, one the most replicated neuroanatomical findings in autism, is reported to be impairment in the Purkinje cells, which are integral to multiple functions of the cerebellum (Sudarov, 2013).

Neurobiological features in autism also include atypicalities in connectivity, which is often assumed to characterize autism (Kana, Libero, & Moore, 2011). These findings have been evidenced by electrophysiology and neuroimaging, molecular genetics, and data processing. However, the specificity of altered connectivity is unknown, although a number of authors have proposed that the most extensively substantiated version of altered connectivity theory and the autistic phenotype supports the premise of global cerebral underconnectivity and local overconnectivity (Kana et al., 2011; Pelphrey, Shultz, Hudac, & Vander Wyk, 2011; Vissers, Cohen, & Geurts, 2012). Of relevance, recent findings from the Autism Brain Imaging Data Exchange (ABIDE), has aided clarification of prior studies of connectivity, confirming both hyper-connectivity and hypo-connectivity to represent features of the autistic brain. In particular hypo-connectivity was more predominant, with influence upon all cortico-cortical connections examined and also influence upon fusiform and superior temporal gyri, hemispheric connections, the insula and paracingulate cortex was proposed. In contrast, hyper-connectivity was found to be more limited, and to affect primarily the parietal cortex and also subcortical nuclei (Lenroot & Yeung, 2013).

Lastly, neurobiological research has outlined innate and adaptive immunological anomalies, linked to autistic pathophysiology with consequences for neurodevelopmental processes, such as neurogenesis, proliferation and synaptic pruning (Onore, Carega & Ashwood, 2012) which we collectively seen to present in both individuals with autism and also their relatives (Parellada et al., 2014). Pervasive neuroinflammation (Fatemi et al., 2012) and increased pro-inflammatory cytokine levels in serum and cerebrospinal fluid (CSF) have also been evidenced, as well as maternal IgG antibodies, which are viewed as

potentially pathogenic during fetal gestation (Lenroot & Yeung, 2013).

Despite, inconsistencies in research concerning neurobiology in autism, the development of new techniques and methods in neurobiology may advance insights into the multiplicity of presentation in autism specifically through quantifying distinct neurobiological systems associated with the varying aspects of autistic symptomology.

### *1.4.3 Cognitive neuroscience theories in autism*

Both the prevalence and heterogeneity of autism has led to extensive theories and empirical research to explain the neurocognitive factors that underlie autistic symptomology.

Divergent hypotheses of impairments in social and non-social cognitive aspects of autism have delineated unitary domain-specific hypothesis, such as Theory of mind (ToM) and also domain-general mechanisms, primarily, executive function (EF) (Pellicano, 2010).

In reference to ToM, this construct concerns the ability to represent another's mental state, including beliefs, intentions and knowledge, and also allows predictions to emerge in relation to the social world, thus enabling adaptive social behaviour (Lombardo & Baron-Cohen, 2011). The proposed cortical regions of the brain associated with social cognition and capacities of ToM, comprise of the superior temporal sulcus, temporo-parietal junction, amygdala, fusiform gyrus, and the prefrontal cortex. These regions have been found to be hypoactive in autism, and hence associated with ToM deficits in ASD (Pelphrey et al., 2011). The research concerning ToM in autism suggest impairments are variable within individuals, wherein, ToM in high functioning individuals is reported to be attained to a certain degree in respect to controlled mentalizing, although implicit and intuitive aspects of ToM are seen to remain impaired (Zwickel et al., 2011).

EF theory, pertains to high level cognitive processes that underpin goal-directed and purposeful behaviour, and also influence abilities in planning, cognitive flexibility, and inhibitory control (Ozonoff, Pennington, & Rogers, 1991). In autism, the cortical regions implicated in impaired EF include the frontal, parietal, and striatal circuitry (Dichter,

2012). Specifically the traits associated with impaired EF, include decreased control of goal-orientated action, impaired planning, perseveration, working memory, impulse control and set-shifting and inhibition of proponent responses (Booth, Charlton, Hughes, & Happe, 2003). EF deficits are also seen to underpin repetitive stereotyped behaviors (Lopez, Lincoln, Ozonoff & Lai, 2005) however, perspectives within research vary, with this behaviour viewed as reflecting a superior performance of routine actions in individuals with autism, underlying a preference for structure and elaborate rituals (Geurts, Corbett & Solomon, 2009).

One further theory pertaining to cognitive neuroscience concerns the preference for global sensory-perceptual processing. This particular mechanism is assumed to integrate information in context to provide meaning (Frith, 2006) and is seen to be frequently present in individuals with autism. This bias in processing 'parts' as opposed to the whole reflects a distinct ability to process information in a more context-independent manner. Furthermore, it is viewed as a cognitive style in autism, facilitating performance in activities requiring a focus to detail. This ability in autism may represent irregular patterns of abilities and in I.Q. performance or alternately, it may reflect a discriminating ability of individual elements, as opposed to failing to integrate information in a gestalt concept (Behrmann, Thomas, & Humphreys, 2006).

Overall, the diverse behavioral symptomology in autism may arise from distinct variation in cognitive and perceptual capacities. Furthermore differentiating between primary and secondary causations of features associated with atypical social and non-social cognition may facilitate insights into the characterization of autism.

The ensuing section focuses specifically on motor symptomology, viewed as a developmental co-occurring condition in autism, with a predominant focus on coordination and postural mechanisms in individuals with ASD.

## *1.5. Neuromotor function in autism*

Within this review, a brief introduction to motor control and its component processes is firstly presented. This inclusion of an outline of motor control is to highlight the importance of considering the interactive and collaborative nature of the neuromotor system in the performance of movement, and importantly, to situate anticipatory or predictive motor behaviour within the context of neuromotor function. Furthermore, this review aims to highlight the complexity of human movement and the need to approach movement from a multidimensional view that encompasses physiological, cognitive and perceptual domains of movement behaviour. A synopsis of impaired motor symptomology in autism follows, and the review concludes with a discussion of the consequences of motor symptomology upon developmental outcomes in autism.

### *1.5.1 Processes of motor control*

The development of human movement and achieving diversity in functional motor skills requires capacities for motor control, comprising of numerous components and processes within physiological, biomechanical, neurocognitive, and psychological systems.

From a developmental perspective, the processes within motor control are not fully constrained within a pre-existing structure at birth. Constant, dynamic adaptions in motor control evolve throughout ontogeny within different environmental settings, via rapid and continuous acquisition of new information streams. Of note, hierarchically organized motor learning processes, which are concerned primarily with ongoing modification of skilled movement, are assumed to be closely intertwined with processes of motor control (Gowen & Hamilton, 2013). Collectively, both these constructs are perceived as representing dynamic continuous processes that exist and adapt across all timescales. Furthermore, motor control and motor learning are seen as dependent on components of motor circuitry, as well as being influenced by cortical and nervous system (NS) integration, environmental stimuli and individual biomechanics (Umphred, 2007).

Conceptually, motor control is essential in formulating neuromotor patterns, which in

turn act to constrain the musculoskeletal system and also the physical laws that govern movement, in the optimization of movement behaviour. Specifically, motor control systems are concerned with orchestrating the body's biomechanical systems, and reducing variation in degrees of joint freedom, to thus enable precision and diversity within functional motor patterns (Elliott, Hayes, & Bennett, 2012). In addition, synergies, or groups of muscles with parallel activation levels, also act to reduce the degrees of freedom within the body's joint systems (Nebel et al., 2014).

A recent review, which investigated computational processes in motor control to contribute to the understanding of disruptions of motor systems in ASD, delineated a series of processes emergent within motor control. These processes are proposed to involve the following components and systems: 1). sensory systems, 2). state estimations of body position, 3). motor planning, 4). feedforward control or prediction, and 5). motor execution (Gowen & Hamilton, 2013). The proceeding discussion concerns these processes in motor control.

Primarily, sensory inputs emerge from visual, tactile and proprioceptive receptors with subsequent interpretation of these inputs, such as, transformation of a retinal image into a representation of the body's position in space (i.e. the environmental setting). A state estimation of the body's position in the environment is then formed, alongside a sensory representation of the qualities of potential targets of interest within the environment (Gowen & Hamilton, 2013). This process contributes to the formulation of motor planning, and is closely linked to multi-sensory integration, which functions at an optimal level if the variability of sensory input is taken into account. This component of motor planning, occurring prior to movement initiation, involves intention and memory and allows a current state estimate, such as a static position of the body to reach a desired state, via sequencing of motor commands (Gowen & Hamilton, 2013). Of note, the evaluation of motor planning is often measured in terms of reaction times prior to movement performance, thus indicating the time period in the forming of an action plan. Important dimensions within motor planning are assumed to be the storage, use and transference of motor knowledge into action, the sequencing of the whole action, or action chaining, and lastly, the kinematics of the action (Noback, Ruggiero, Demarest, Strominger, 2005).

The process of feedforward control and prediction, constituting a motor command or efference copy transcribed to a forward model, to thus generate a prediction of the sensory consequence of action follows the processes above. This sensory prediction is compared to incoming sensory input, to allow detection of movement errors (Wolpert &Flanagan, 2001). Analysis of predictive motor control is seen to occur by examining rapid movement corrections prior to feedback being available. Notably, this predictive process can be measured by unloading paradigms, such as the BMLL task. Lastly, measuring the sensory consequences of forward models, is carried out in tickling and force cancellation paradigms, whereby the stimuli is represented as weaker, in a self-generated event and also predictable, as opposed to an externally generated stimuli (Blakemore et al, 2000).

Of note, feedback systems rely on peripheral input, such as intrinsic (i.e. sensory receptors) or extrinsic (i.e. visual or verbal information) feedback in recognizing and correcting errors during movement performance. This process however is slower than feedforward control, thus, dependency on this system alone would result in slow and inefficient movement behaviour. Together, both feedforward and feedback systems are proposed to develop through experiential learning and through ongoing practice (Noback, Ruggiero, Demarest, Strominger, 2005; Umphred, 2007).

Subsequent to feedforward control, the final process of motor control involves motor execution, comprising of a series of motor commands, which are sent to peripheral nerves onto the associated musculature, via the motor cortex (Shibasaki, 2012). Importantly, motor execution is influenced by output variability, for example, errors may ensue in relation to movement endpoint, or time increases on movement correction, in the event of increased output variability. Additionally, precision in timing, to a millisecond scale of agonist and antagonist musculature, also influences movement execution, thus altered timing may affect position, orientation and movement speed of the body's limbs (Hore, et al., 1996). Furthermore, imprecise timing may be a precursor of dysmetric movement, affecting both spatial and temporal dimensions of movement, for example duration, acceleration, and peak velocity.

In sum, human movement subserved by multiple systems and processes, vis-à-vis motor control requires elaborate neuromotor, cognitive and perceptual integration to achieve

precise movement behaviour. A disruption in anyone of these components or process would eventuate in cascade effects on associated mechanisms, and thus, alter the quality and diversity of human movement behaviour.

The following account outlines the range of motor symptomology in autism, examining the specific impairments of perceptual-motor function, praxis, imitation, coordination and postural control in individuals with autism.

### *1.5.2 Developmental profile of motor symptomology in autism*

The existence of atypicalities of motor behaviour in autism has been recognized since Kanner's original description in 1943 (MacNeil & Mostofsky, 2012). Furthermore contemporary research involving multiple studies, case reports and case-control studies has evidenced substantial motor impairments and atypicalities across the spectrum of autism. Additionally, despite variation existing in motor abilities across individuals with ASD, motor symptomology is viewed as highly prevalent (Bhat et al., 2011; Gowen & Hamilton, 2013; Mostofsky & Ewen, 2011; Stanley-Cary, Rinehart, Tonge, White, & Fielding, 2011) with the incidence of motor impairments ranging between 50-100% (Haswell, Izawa, & Dowell, 2009; Lane, Harpster, & Heathcock, 2012). Importantly, accumulating evidence also suggests the presentation of motor symptomology, to be one of the earliest predictors of ASD diagnosis (Nebel et al., 2014).

In examining the specificity of motor symptoms in ASD, standardized neuromotor evaluations of autistic children and adults have revealed measurable motor impairments in gross and fine motor skills, postural control, coordination, imitation and praxis ( Bhat et al., 2011; Johnson et al., 2013; Lane et al., 2012). Impaired sensori-motor integration (Gowen & Hamilton, 2013) and qualitative motor performance difficulties in motor planning and gait patterns are also frequently reported in individuals with ASD (MacDonald, Lord, & Ulrich, 2013; Rinehart et al., 2006).

In the developmental profile of motor impairments in infants who later were diagnosed with ASD, the following deficits have been evidenced; abnormal muscle tone, postural

asymmetry in supine and prone (Nickel, Thatcher, Keller, Wozniak, & Iverson, 2013), abnormal reflexes, motor delays in the acquisition of sitting skills, oromotor deficits (Teitelbaum,Teiltebaum, Nye, Fryman, & Maurer, 1998) and excessive stereotypical object play ( Bhat, Landa, & Galloway, 2011). In addition, a study concerning early motor identification markers in ASD, found at 14th months postpartum, that children later diagnosed with autism had a slowing in development, and by 24 months, marked deficits in motor function presented in autistic children in comparison to typically developing children and children with language delay (Charwarska, et al., 2007; Provost, Lopez, Heimerl, 2007).

By the second year of age in children with ASD, delays in onset of walking is common, as well as difficulties in balance and slower speed in timed movements (Ozonoff et al., 2008). Specifically, gait is characterized by later onset of atypical features, including reduced heel-toe pattern, reduced reciprocal arm movement, and waddle- type gait pattern. In addition, fine motor delays were found in infants at approximately 14 months of age. Delays have also been reported in upper limb function, included pointing, reaching, clapping, and playing with puzzles and block toys. Furthermore, in the second year of life, motor stereotypies, are common traits in children with autism, characterized by spontaneous repetitive movements such as arm flapping and rocking (South, Ozonoff, McMahon, 2005).

Later in maturation, variable features of neuromotor function in autism include impaired tone, posture, balance, fine motor skills, gross motor skills, coordination, gait atypicalities, (Forti et al., 2011), motor planning, neurological soft signs (NSS) (De Jong, Punt, De Groot, Minderaa, & Hadders-Algra, 2011), altered movement patterns and impaired performance of skilled gestures (Gidley Larson & Mostofsky, 2006; Jasmin et al., 2009; Lane, Harpster, & Heathcock, 2012). Motor coordination impairments are also reported in up to 80% of children with autism, and notably, are viewed as highly correlated with both IQ and severity of autism (Hilton, Zhang, Whilte, Klohr, Constantino, 2012). The aforementioned meta-analytic study on motor function in ASD also evidenced significant impairments in both lower and upper extremity motor performance in autism, with

greater impairments presenting in functional patterns of the upper extremities (Fournier et al., 2010).

In school aged children with ASD, a range of motor impairments present, including difficulties in manual dexterity, balance, ball skills and graphomotor skills (Provost, Lopez & Heimerl, 2007). Postural sway, in medio-lateral, anterio-posterior and normalized sway has also been shown to be significantly greater in comparison to typically developing controls in school aged children with autism (Fournier et al., 2010). During this developmental stage, motor planning deficits are also evident in children with ASD, wherein motor tasks within an overall action were treated independently, reflecting a deficit in translating motor intention into a global motor action (Downey & Rapport, 2012). Interestingly, children with autism of ages between 4-6 years have shown difficulty in defining the goal of an action, indicating difficulties with motor planning. Principally, the difficulty appeared to lie in chaining multiple motor tasks into a complex motor actions (MacDonald et al., 2013).

Additionally, from ages 7 to 32 years, findings in motor symptomology in ASD comprise of impaired coordination of upper extremities in visuo-motor tasks and in tasks involving manual dexterity, as well as lower limb coordination deficits, with consequences for speed, agility and balance (Bhat et al., 2011). Overall, however the specificity of motor deficits in ASD in later childhood and adult stages as well as siblings at risk, are understudied, thus a more detailed understanding of pervasive motor impairments in later developmental stages is required.

### *1.5.3. Perceptual motor processes*

Perceptual motor processes represent foundational capacities in utilizing sensory information to perform skilled, purposeful motor actions. In integrating perceptual-motor stimuli, an individual is able to determine their own action capabilities in multiple activities within various environmental settings. To illustrate, the integration of perceptual and motor processes is required, for example, in evaluating when to cross a

road (Adolph & Berger, 2006) and also in the coordination of movements when interacting with another in different environments (Chang, Wade, & Stoffregen, 2009).

Importantly, this integrative process involves an association between actions and sensory feedback which allows the prediction of sensory consequences to occur via motor commands, within an essentially self-formulated process (Izawa et al., 2012). Thus, selection of an action plan to achieve a goal of an action depends on predicting sensory consequences relative to oneself. The adaptation of movements via internal representations therefore contributes to enhanced perceptual skills, and the subsequent refinement of skilled movement behaviour.

Taken together, the aforementioned processes are emblematic of an interrelationship of perception, cognition and action. Of relevance, this interrelationship may also be foundational in the abilities of imitation and subsequent learning from another's actions as well as the generation of interpretations of the intention of another's actions, occurring via observation (Rizzolatti, Fogassi, & Gallese, 2001). Specifically, this premise assumes that internal representations using a feedforward format, enables extrapolation and inference of others' actions, via mentalizing capacities (Aziz-Zadeh & Damasio, 2008; Klin, Jones, Schultz, & Volkmar, 2003; Lombardo et al., 2010). Thus, the formation of internal models could be assumed to subserve the development of perceptual models of the world and aspects of cognition (Mostofsky & Ewen, 2011). Overall, underlying the capacity for human movement, the existence of a functional association between hierarchical systems, perceptual and predictive mechanisms, as well as the body's biomechanical systems seems intuitive, however, further investigations are necessary to fully support this perspective.

In individuals with autism, sensory processing difficulties are often reported as well as atypical perceptual functioning. A recent study examined atypicalities in 208 pre-school children with autism, who were sub grouped according to autistic symptoms and cognitive levels. Findings showed 76% of the group presented with at least one atypical sensory modality, though differences varied in respect to subgroups, wherein high frequency of atypicalities occurred in the subgroup of classic autism without learning

disorders, and in the Asperger Syndrome group (Klintwall et al., 2011). Furthermore, presentation of sensory modulation disorders (SMDs), or difficulties in regulating and organizing behaviour in response to varied sensory input, such as proprioceptive, vestibular, visual, tactile, and olfactory input, are common in both children and adults with autism. Distinct categories of SMDs have been described, pertaining to *1).* under-responsive or slow response to sensory input, (i.e. pain or responding to own name), *2).* over-responsive to stimuli, an excessive or prolonged response (i.e. covering ears), and 3). sensation-seeking, or craving stimuli for prolonged periods (i.e. arm flapping) (Baranek, 1999, Miller et al., 2007, Baranek, 2006, as cited in Bhat et al., 2011). Of relevance, the presence of altered sensory processing has been shown to be positively correlated with motor performance primarily in relation to postural control and coordination (Liu, 2013). In addition, the severity of SMDs has also been shown to have a direct correlation with autistic functioning, including communication and autism severity ( Bhat et al., 2011).

An additional study, examining affordance perception or the ability to perceptually integrate the physical abilities of 'self' with one's own environment, evidenced marked deficits in autistic participants compared to controls, in reference to information regarding their own bodies' action capacities, to visual details about the environment. Of relevance, the degree of impairment in affordance perception strongly predicted the degree of socio-communicative impairments in autistic group (Linkenauger, Lerner, Ramenzoni, & Proffitt, 2012).

In sum, research concerning sensory and perceptual-motor processes in autism may be of value in the development of therapeutic interventions, which are generally underemphasized in treatment strategies. Also, the above findings suggest intervention approaches encompassing sensory and perceptual targets may have secondary effects upon the central features of ASD.

### *1.5.4 Praxis and Imitation*

Human movement performance, can be delineated by examining praxis or the ability to plan and execute a motor programme, and also by examining imitation, or emulating an

observed action in which an individual cognitively deconstructs the action into a hierarchy of goals based on functionality (Mostofsky & Ewen, 2011). Both the skills of praxis and imitation, necessary for precision in human movement behaviour, require intact and optimal functioning of the sensorimotor system, which in turn depends on the aforementioned processes and components of motor control.

Firstly, praxis is comprised of primary components that include - 1). ideation, or the generation of an idea of an action to be performed in the environment and 2). ideomotor, referring to planning or arranging an action programme, followed by 3). the execution of the movement sequence. Parietal - frontal connectivity is seen to be play a role in the operations of praxis, and disruption of these structures is assumed to be associated with both ideational and ideomotor apraxia (Shibasaki, 2012).

In studies of praxis in autism, impairments of skilled goal-directed motor gestures on command and during imitation have been evidenced (MacNeil & Mostofsky, 2012). Specifically, deficits consist of a slower preparation time in the execution of goal-directed movement (Rinehart, Bradshaw, Bereton, Tonge, 2001), impaired sequencing, vision, consequence prediction, motor planning and execution (Vernazza-Martin et al., 2007), deficits in force or timing of movement, altered amplitude, inaccurate limb orientation (Gowen & Hamilton, 2013) and also impaired functional use of tools (Haswell et al., 2009). Together these deficits have been described as consistent with developmental dyspraxia ( Bhat, Landa, & Galloway, 2011; MacNeil & Mostofsky, 2012). Further findings from a recent study of children with autism, examining praxis recognition, or the ability to recognize the skilled gestures of others, indicates deficits in this aspect of praxis, and of note, findings suggest correlations with social impairments (MacNeil & Mostofsky, 2012).

Secondly, in examining skills in imitation, this ability is seen to be pivotal in learning throughout ontogeny, wherein imitation is viewed as foundational in - *1).* cognitive development, *2).* developing an understanding of the physical world, as in cause-effect relations, *3).* transmission across generations of behaviour and customs within a social context, *4).* socio-emotional development and *5).* theory of mind (Edwards, 2014). In addition, capacities in imitation are assumed to fast track acquisition of skills, thus, the

existence of imitation deficits indicate the implementation of a less efficient mode of learning, such as trial and error learning (Meltzoff et al., 2009). However, the measurement of imitation abilities is problematic, for example, during examination, actions may vary in relation to performance which has implications for quantifying results in relation to standardized comparisons. Furthermore, memory, attention, motor control, low IQ, poor spatial reasoning, and social motivation may underlie imitation deficits (Edwards, 2014) and although these deficits are a potential precursor of imitation, they maybe a consequence of imitation deficits.

In relation to the neural basis of imitation, the mirror neuron system (MNS), comprising of the inferior frontal gyrus , the premotor cortex, inferior parietal lobe, and the somatosensory cortex (Braadbaart, de Grauw, Perrett, Waiter, & Williams, 2014) is seen to underlie abilities in imitation. Impairments in the MNS has been proposed to contribute to imitation symptomology in ASD by numerous studies, however debate continues as to the existence of a disruption of the MNS in autism (Enticott et al., 2013). In addition, the debate on the association between MNS and autism has recently diverted from the primary focus on higher cognitive processes, such as understanding false beliefs, to more fundamental processes concerning infant social learning and understanding (Vivanti & Rogers, 2014).

Regardless of MNS controversy, multiple studies describe diverse impairments in imitation in autism, evident from infancy and persisting into adulthood. Impairments in imitation include postural, orofacial, and manual function, as well as reversal patterns, - such as when a child copies a palm movement that faces forward, they imitate with their own palm facing towards themselves, as opposed to away from themselves (Mostofsky et al. 2006). Alternately, in body-part-for tool actions, an example of error may occur when the child uses the hand as a toothbrush to demonstrate its use, rather than showing a grasp pattern ( Bhat et al., 2011). Individuals with autism also demonstrate errors in imitating purposeless gestures, or performing an uncommon action with familiar objects as well as imitating difficulties within the expressive qualities of an action, such as generation of appropriate force (Edwards, 2014). Findings however are inconsistent, in

regard to the nature of imitation in autism, existing in part from inconsistencies of operational definitions of imitation, associated with varying research designs.

Finally, impaired imitation capacities in autism have recently been characterized as a social learning disorder, wherein difficulties in social engagement undermine opportunities for social learning. Thus, encompassing aspects of social learning, and the mechanisms of the MNS, may play a role in illuminating learning processes and also devising strategies for learning in individuals with autism (Vivanti & Rogers, 2014).

### *1.5.5 Motor coordination and bimanual coordination*

The emergence of coordination, dependent on feed-forward and feed-back mechanisms that subserve motor commands, which in turn direct multiple effectors, such as joints, limbs and muscles in achieving a goal, involves many levels of motor control and also motor learning (Diedrichsen, Shadmehr & Ivry, 2009). From a developmental perspective, during the ages of 5-10 years, the affordances and constraints of the musculoskeletal system, alongside task demands and environmental factors, act to influence the refinement of coordinated movement. Qualitative changes present in coordination, while underlying motor skills become more controlled, and reach higher levels of complexity of skilled activity. During adolescence, improved quantitative performance and qualitative changes in coordination skills emerge, influenced by perceptual development and information processing. Manipulative skills in adolescence often resemble adult's skill level, and dexterity for complex tasks during this developmental stage demonstrates greater proficiency and precision (Umphred, 2007).

Further refinement of skill and involvement of complex processes, including high levels of synchrony, attentional resources and elaborate programming, is required to achieve precision in bimanual coordination, an essential capacity in the performance of many activities of daily living (Isenhower et al., 2012). In particular, accuracy in bimanual coordination is required in events where the homologue muscle in the contralateral limb

is performing an independent, distinct movement, such as in playing a musical instrument (Zanone, Monno, Temprado, & Laurent, 2001).

Of further relevance, achieving diversity of spatiotemporal configurations in bimanual coordination patterns requires modulation in accordance with the type of sensory modality involved, the degree of sensorimotor integration, the constraints of task dynamics, the context of the task, and also the environment in which they occur. To illustrate, in relation to task strategies, individuals may differ in terms of assigning priority to either visual or proprioceptive input. Additionally in clinical populations, individuals may differentially rely upon prefrontal recruitment, to compensate for cortical atypicalities, pathologies, or dysfunction (Gooijers & Swinnen, 2014a).

Perceptual-cognitive processes, including symbolic cue decoding (Diedrichsen, Hazeltine, Kennerley & Ivry, 2001), target detection, delineating movements in terms of target configuration, planning of movement trajectories, saccade production, and perception of visual input (Janczyk, Skirde, Weigelt & Kunde, 2009), are also seen to direct bimanual coordination, wherein these processes act in the limitation of the neuromuscular system, thus functioning as constraints. The origin of these constraints before the onset of movement, are seen to specifically emerge from target detection and planning of movement trajectories and during execution of movement, constraints are assumed to arise from intrinsic muscle factors. Notably, modulation of constraints is assumed to occur via visual perception of unfolding movement patterns and also the expression of constraint mechanisms is proposed to be differentially sensitive to perceptual, cognitive and motor demands of various task conditions (Procacci & Stanford, 2013).

In studies of motor coordination in autism, recent research has proposed that up to 80% of children with autism present with coordination impairments (Hilton, Zhang, Whilte, Klohr & Constantino, 2012), thus reflecting findings within Fournier's (2010) meta-analysis of motor coordination in ASD, which delineated coordination impairments as a cardinal feature of autism. Specifically, in Fournier's study the predominant motor symptomology in ASD was proposed to be impaired motor coordination of the upper and lower limbs, with impairments seen to be more prevalent on examination when motor

performance was dependent on postural control. Importantly, coordinated movement of the head and hand, and reflex inhibition were assumed to limit skills in hand manipulation, with consequences for accuracy in bimanual coordination performance.

Further studies examining motor coordination in autism, have revealed wide range of impairments including, lack of motor fluidity (Behere, Shahani, Noggle, & Dean, 2012), specific difficulties in multi-joint coordination during locomotion (Kohen-Raz, 1992; Vernazza-Martin, 2008), upper extremity coordination deficits in children with autism (Gernsbacher, Sauer, Geye, Schweigert &Hill Goldsmith, 2008), motor delays in manual dexterity in children with ASD (Lane et al., 2012), reduced degree of handedness, decreased consistency of hand preference (McManus, Murray, Doyle, Baron-Cohen, 1992) and rhythmic bimanual coordination differences, primarily in anti-phase patterns as shown in a recent study in children with ASD (Isenhower et al., 2012). Also research which examined developmental coordination disorder (DCD) rates among preschool and school-age girls with ASD, found that a large minority of school-age girls and a majority of preschool girls met full diagnostic criteria for DCD (Kopp, Beckung, & Gillberg, 2010).

Collectively, these findings indicate that multiple coordination deficits, subserved by a range of neural and cognitive mechanisms, present in children with autism. At present it is unclear whether these coordination deficits and associated consequences persist throughout the stages of adulthood.

### *1.5.6 Postural control*

Postural control, underlying movement coordination, influences the precision and accuracy of human movement behaviour. Functionally, the control of posture relies upon internal representations or sensori-motor programs, to enable stabilization of joints systems during movement. This process occurs via co-activation of agonists and antagonists of various joint structures of the body. The distinct elements of postural control include: - 1*).* verticality with regard to gravity, and the maintenance of balance against internal and external perturbations, *2).* anticipatory postural control, involving a 'postural preset', wherein trunk stability is maintained to allow skilled movement of the

limbs to occur (of note, the recognition of stimuli and potential destabilizing forces, as well as memory is required within this element), *3).* tonal level or the existence of hypertonicity or hypotonicity in certain muscle groups which compromise postural control, *4).* sequencing of movement patterns, with reference to skills in praxis, and *5.)* multi-sensory integration (Umphred, 2007). In addition, vestibular, proprioceptive and visual systems are seen as contributory to postural control (Mohapatra, Krishnan, & Aruin, 2012; Travers, Powell, Klinger, & Klinger, 2013). Impairment or disruption in any of these mechanisms is assumed to challenge the control of posture, with subsequent deficits in motor skills and thus, coordination patterns.

In examining static and dynamic postures, humans experience balance perturbations that impact on the body's state of equilibrium, and these perturbations may be internal, that is, created by self-initiated movements of the body and limbs, or perturbations may be external, where a force is imposed on the body from the external environment (Santos, Kanekar, & Aruin, 2010). Thus to sustain a state of equilibrium, as well as achieving continuous automatic adjustments prior to and during movement, humans require precision in postural control (Tomita, Fujiwara, Mori, & Sakurai, 2012). To achieve this, an individual may need to reduce muscle activity that is too high to thus allow accuracy in performance of movement sequences, or augment activation when muscle activation is too low, thus enabling a movement sequence to emerge. Notably, both these processes are required to evolve in conjunction with the appropriate timing of postural responses (Krishnan, Latash, & Aruin, 2012).

In autism, there is minimal research regarding the features of postural control across varying developmental stages, thus an understanding of early clinical markers for autism within the domain of this motor feature is limited. This lack of research exists even though extensive impairments in physical structures, and subsequent motor functions are seen to affect the control of posture, as evidenced in recent studies of children with ASD (Cheldavi, Shakerian, Nahid, & Boshehri, 2014; Fournier, Amano, Radonovich, Bleser, & Hass, 2014 ).

Postural control in infants with autism risk status (i.e. infant siblings of children with autism) was recently examined in a study, with findings reporting the presentation of

head lag, a predictor of developmental disruption in cerebral palsy and preterm populations, to be significantly correlated with ASD at 36 months of age, and also to present more commonly in high-risk infants compared with low-risk participants (Flanagan, Landa, Bhat, Bauman, 2012). The authors suggest that early motor deficits, vis-à-vis, head lag may be a pre-clinical indicator in autism, and may also precipitate socio-communicative features in ASD, such as reciprocal affect, and qualitative synchronous movement occurring in interpersonal interactions (Bhat, et al., 2011).

Also a study in children with HFA, comprising of 19 boys ages 10-15 years, compared to 28 matched controls which examined the interference of visual and auditory tasks on postural control in standing, showed higher levels of postural instability in the children with HFA compared to controls (Memari, Ghanouni, Shayestehfar, Ziaee, & Moshayedi, 2014) . The evidence suggested that high levels of postural sway in the autistic children was due to impaired integration of input from vestibular, visual and somatosensory systems. Preferential use of the somatosensory system to maintain balance has also been described as a common characteristic in ASD (Molloy, Dietrich, &Bhattacharya, 2003). In the paper by Fournier et al., (2014) postural control in children with autism compared to controls was examined via analysis of center of pressure (COP). Fluctuations in COP and postural control dynamics in the children with ASD showed more repetitive patterns in COP, thus suggesting decreased complexity of postural control in comparison to the typically developing children. The authors proposed that the more restricted control of posture may indicate a link between postural instability and stereotypic behaviour in ASD, and therefore provide insights into autism neurobiology.

Overall, the findings from the studies collectively suggest autism is associated with a range of deficits in postural control, underpinned by a number of mechanisms, which have secondary effects upon associated motor skills and potentially central features of ASD. Thus, early interventions aimed a facilitating postural mechanisms in children with autism may contribute to optimizing developmental motor skills in individuals with autism.

The outline below overviews APAs, a sub-component of postural control, which is later discussed in detail in the context of the study experiment within chapter 2.

*Overview of APAs*

In achieving goal-directed volitional movement, the aforementioned mechanisms of postural control are essential. However, a further component of postural control is required to enable accuracy and precision in movement performance. This component is defined as anticipatory behaviour, which plays a central role in the prediction of consequences of planned motor actions (Jover, Schmitz, Centelles, Chabrol, & Assaiante, 2010). This anticipatory behaviour originates through the generation of APAs, representing adaptions in background muscle activity preceeding volitional movement that function to minimize disruptions to stability, via predictions of internal and external mechanical pertubations arising through movement (Shiratori &Aruin, 2007).

In the context of motor control theories, APAs are intricately associated with sensori-motor programmes or internal action models, and also forward model predictors. Collectively, these processes contribute to the formation of estimates concerning action outcomes. Proceeding this process, is the construction of an action plan, to sustain and maintain aspects of postural stability, which essentially underpin the production of elaborate coordinated movement (Barlaam, Fortin, Vaugoyeau, Schmitz, & Assaiante, 2012b).

As APAs emerge prior to the onset of movement, this mechanism is assumed to be centrally controlled. Additionally, modulation of APAs is seen to occur via high-level cognitive processes, such as attention and anticipation (Tomita, Fujiwara, Mori, & Sakurai, 2012) and biomechanical factors, such as speed of movement ( Mochizuki, Ivanova &Garland, 2004), and start and final positions of the body (Aruin & Shiratori, 2003) are proposed to influence the charateristics of APAs.

The discussion following outlines the neurophysiological basis of motor impairments in autism, examining potential neural correlates associated with impaired bimanual coordination and postural control.

### *1.5.7 Neurophysiological basis of motor symptomology in autism*

While numerous studies have delineated the range of neuromotor impairments in autism, research has not established a definitive aetiology. Thus, debate continues in respect to proposed anomalies in neural circuits and cortical regions, and notably, this debate persists despite specific clinical neurological dysfunction in autism remaining undefined (De Jong et al., 2011). However, several neural correlates and also divergent paradigms have emerged to elucidate atypical motor behaviour in autism.

Firstly, the neural correlates pertaining to impaired motor function in ASD based on findings from neuroimaging studies have revealed the following anomalies: - 1). Cerebral cortex- frontal, temporal, parietal lobes showed hyperplasia of both grey and white matter and abnormalities of corpus collosum and ventricular system (Carper & Courchesne, 2005), 2). Cerebellum- anomalies in the shape of the vermis and cerebellum, and loss of purkinje cells (Becker & Stoodley, 2013), 3). Basal ganglia- increased volumes of putamen and caudate nucleus, (Hollander, Anagnostou, Chaplin, et al., 2005), 4). Thalamus - increased volume (associated with repetitive behaviors) (Tsatsanis et al., 2003),and 5) Hippocampus - reduced size and atrophy (linked to spatial awareness) (Saitoh, Karns, and Courchesne, 2001). In addition, atypical activation responses in the supplementary motor area (SMA) have been evidenced in healthy populations who presented with high scores on the Autistic Quotient (AQ) (Puzzo, Cooper, Vetter, & Russo, 2010).

Furthermore, functional magnetic resonance imaging (fMRI) studies have revealed differential brain activation associated with motor performance in children with autism, suggestive of a reliance on alternative pathways (Verhoeven, De Cock, Lagae, & Sunaert, 2010). Also of relevance, a recent study examining the functional organization of the motor cortex in autistic children compared with controls, found atypical functional segregation in the primary motor cortex, which is concerned with both motor control and motor coordination. The authors suggested that the consequence of this atypical segregation may result in impairments in generating complex synergistic muscle activity, required for the performance of highly skilled movements (Nebel et al., 2014).

Secondly, paradigms that have been mapped onto dysfunctional motor systems in autism outline deficits in a number of processes including multisensory integration (Gowen & Hamilton, 2013), sensory feedback and motor preparation - characterized by reduced anticipation and planning (Behere et al., 2012), atypical functional segregation in regions concerned with motor coordination (Nebel et al., 2014), alterations in motor circuits, gross brain dysfunction, and behavioral byproduct of the interactions between motor function and other core features of ASD ( Fournier et al., 2010). It is noteworthy that distinct motor processes have been proposed to underlie differing motor skills in autism, for example, posture is proposed to rely on processes predicting the consequences of movement, while fine motor skills are seen to rely on motor execution, thus indicating that further investigation and divergent approaches are required to fully explain which motor processes are impaired (Fournier et al., 2010).

*Potential neural correlates of impaired bimanual coordination in autism*

Despite extensive research into bimanual coordination, neither the core neural mechanisms nor a unifying framework involved in these complex movement behaviors has, as yet been defined. Accumulating evidence however, indicates that the supplementary motor system (SMA) and the pre-SMA (i.e. the anterior aspect of the SMA) play predominant roles in bimanual coordination specifically in functional specialization of motor planning, movement execution, and receiving and processing of movement cues (Wu, et al., 2010). In particular, the SMA, is assumed to subserve the performance of movement sequences, predominantly in the absence of external cues (Rothwell, 2012). In addition, both regions of the SMA are seen to influence movement that is 1). internally generated, or externally triggered, as well as 2.) teaching new movements, 3). movement inhibition, and 3). cognitive control of extended duration and complex movements (Wilson, et al., 2014).

Structurally, the 2 distinct regions of the SMA; the SMA proper - comprising of the medial frontal granular cortex anterior to the primary motor cortex, with direct projections to the spinal cord, differs from the pre-SMA - which is structurally more distant from the primary motor cortex, receiving projections from both the prefrontal cortices, and

cingulate motor regions (Hoshi & Tanji, 2004; Nachev, Kennard, & Husain, 2008; Tanji, 1994). Findings have indicated that the pre-SMA functions in more complex and abstract movement patterns and this region is assumed to be a center for performing real-time spatiotemporal transformations, consistent with the prescribed involvement of this region in mental rotation and other cognitive functions, as outlined in previous studies (Leek & Johnston, 2009). In addition, recent research has also shown that the pre-SMA preferentially receives multi-sensory input, comprising of somatosensory, proprioceptive and visual input, and this region is proposed to carry out complex transformations which may contribute to future movement programming, and also guide movement outcomes via interactions with the SMA proper (Hoshi & Tanji, 2004; Leek & Johnston, 2009; Makoshi, Kroloczak, van Donkelaar, 2011).

In addition, disorders of the basal ganglia are associated with impaired coordination, as well as a number of symptoms involving presence of extraneous movement, altered muscle tone, postural stability and motor control. This range of symptoms is the result of the basal ganglia circuitry, which has extensive connections to the motor cortex, thus the basal ganglia can affect the motor system at many levels. Specifically, the basal ganglia is implicated in internally generated movement, as well as complex movements and postural reflexes and adjustments, via analyses of cortical input to predict motor actions (Estes et al., 2011).

The corpus callosum (CC) and associated subcortical structures (Gooijers & Swinnen, 2014b), has also been examined within the context of bimanual coordination, wherein the anterior part of the CC in particular is implicated in bimanual coordination. Insights into links between CC structures and bimanual coordination have emerged from studies on split-brain patients in reduction of epilepsy, wherein a reduced accuracy and slowness in bimanual coordination presented post surgically. (Preilowski, 1972) Additionally, neuroimaging including transcranial magnetic stimulation (TMS) and diffusion magnetic resonance imaging has enabled characterization of microstructural properties of the CC, thus providing knowledge of the role of the CC in various behaviors, including bimanual coordination (Bonzano et al., 2008). However, Gooijers & Swinnen (2014b) outline that a number of cortical regions contribute to bimanual condition, thus bimanual coordination

though reliant upon the processing and transmission functions of the CC, also relies on other neural substrates to attain precision in this skill.

Also influential in the spatial accuracy and also temporal coordination of motor behaviour, is the cerebellum (Becker & Stoodley, 2013) which is seen to adapt movement in accordance to feedback, by comparison of sensory input with motor output, wherein the cerebellum uses information to update associations between motor commands and predicted sensory consequences (Rothwell, 2012). In addition the cerebellum is influential in reflex responses, anticipatory planning, and visual spatial organization (Fatemi et al., 2012). Importantly, a recent study, found causal evidence of cerebellar Purkinje cell activation in the induction of motor learning, concluding that Purkinje cells, in conjunction with climbing fibers, may enhance motor circuit capacities in learning responses to differential cues (Nguyen-Vu et al., 2013). Of note, lesions of the cerebellum produce multiple motor impairments including dysmetria, ataxia, dysarthria and oculomotor dysfunction (Manto & Pandolfo, 2002). Finally, the premotor-parietal network is also shown to be associated with the temporal and spatial precision of bimanual tasks (Diedrichsen et al. 2006).

Neural anomalies in the regions of the SMA, basal ganglia, cerebellum, the motor cortex, and the CC, proposed to present in individuals with autism, may thus play a causal role in impaired sensori-motor integration, motor planning and execution, which may ultimately contribute to deficits in motor performance and coordinative skills, evidenced in individuals with autism.

*Potential neural correlates of impaired APAs in autism*

To date, the definitive neural basis of APA generation, associated with centralized motor planning is inconclusive, although, several regions have been proposed to play a role in APA function. These regions comprise of the contralateral primary motor cortex, premotor area, SMA, (Izawa et al., 2012; Nayate, Bradshaw, & Rinehart, 2005; Rothwell, 2012; Sudarov, 2013), pontomedullary reticular formation of the brain stem (Lomond et al., 2013), basal ganglia, parietal cortex (Barlaam et al., 2012b) and ventral premotor

cortex (vMPFC) – which is assumed to influence spatial coding of stimuli to ensure referencing of the body in space (Moseley et al., 2013).

Specifically, the basal ganglia-thalamo-cortical motor circuit is posited as influential in the role of preparation of motor programs via mediation of APAs. The precision of temporal organization of APAs in bimanual tasks, is assumed to depend on precise connectivity between the neostriatum and the SMA, via the thalamus (Barlaam et al., 2012b). Of note, a recent study measuring premovement brain activity in conjunction with upper extremity APAs during a BMLL task, showed the additional involvement of the pre-and post-gyri, middle and medial frontal gyri, alongside activity of the parietal lobes, thalamus and the basal ganglia (Ng, Sowman, Brock, & Johnson, 2011).

As yet, there is minimal research of the neural basis of APAs function in autism, although an investigation of autism traits and EEG activity in the SMA, showed a low beta ERD over the SMA in participants with high traits of autism, assumed to represent deficits in chain-based mechanisms, and notably responsible for impaired understanding of motor intentions (Puzzo, Cooper, Vetter, & Russo, 2010).

In addition, a number of neural mechanisms underpinning postural deficits in autism have been proposed specifically comprising of the following; - 1.) action chaining, - reflective of dysfunction in hierarchical action planning (Cattaneo et al., 2007), 2.) low-level internal representations that contribute to movement execution, 3.) timing parameters - concerning adaptive feedback-dependent mechanisms (Bhat et al., 2011; Schmitz, Martineau, Barthélémy, & Assaiante, 2003) and 4.) absence of ERD- indicating a central deficit in anticipation of perceptual consequences and motor planning (Martineau, Schmitz, Assaiante, Blanc, & Barthélémy, 2004).

Overall, various neural substrates and associated mechanisms appear to be associated with postural impairments in autism, however, further investigations are required to delineate the specific causation of postural atypicalities, and also to decipher the role of postural impairment on associated motor characteristics in ASD.

### *1.6 Discussion*

Autism, presents with a diverse range of impairments in motor function across all ages and across the spectrum of ASD. In sum, impairments manifest in skills relating to gross motor and fine motor function, coordination, postural control, praxis, imitation, and perceptual motor skill, which together have potential effects on the development of core autistic features. The discussion to follow aims to highlight that investigations of motor symptomology and potential associations with developmental outcomes in autism, is of importance principally in advancing the conceptualization and clinical understanding of ASD, in addition to informing diagnostic procedure (Dowd, Rinehart, & McGinley, 2010).

Firstly, delays and deficits in postural mechanisms are assumed to influence development in both physical and cognitive domains, with consequences for motor coordination, body awareness, spatial awareness, social skill capacities, learning and academic skills (MacDonald et al., 2013). Specifically, postural delays are of significance when considering normative developmental literature, which outlines postural advancement as scaffolding emergent developmental opportunities during the period of infancy, and also enhancing progressive and sophisticated interactions in the social environment. Thus, in autism, postural delays in infancy would reduce accessibility for exploration and learning, as well as affecting engagement in social environments (Nickel et al., 2013).

Additionally, motor development is proposed to be closely associated with outcomes in learning, as well as social and psychological development (Rinehart & McGinley, 2010). Furthermore, the acquisition of motor skills occurring via repetition, or procedural learning, is proposed to be associated with development of play skills (Clearfield 2011), communication and social development (Ullman, 2004) and also adaptive behavioral skills. Notably, a recent study examined the relationship between motor skills and social communication skills in a large sample of autistic children, and found children with greater deficits in motor function to have greater social communication deficits (motor skills significantly predicted calibrated autism severity ($p < .05$) (Macdonald, Lord, & Ulrich, 2014).

Correlations between motor capacities and cognitive functions has also been evidenced by extensive research, with findings suggesting a relationship between motor function and visual and motor imagery, mental rotation, temporal judgment (Behere et al. 2012), perception, executive function, (Williams, et al., 2006) working memory ( Bhat et al., 2012; Piek, Gasson, & Summers, 2008) literacy and numeracy (Bobbio, Gabbard, Goncalves, Baros Filho, & Morcillo, 2009). In autism, impairments in a number of these cognitive abilities have been outlined, thus suggesting an association between motor function and cognitive function in autism. Furthermore, perceptual-motor function, integral to motor development and independence skills, is often found to be atypical in individuals with autism. Of note, impaired perceptual-motor skills are proposed to constrain socio-communicative and physical interactions during critical periods of ontogenetic development (Fournier et al., 2010). Taken together, the aforementioned findings suggest delays and impairments in postural mechanisms and motor function may play a causal role in other developmental features of ASD. Thus, future investigations of motor skills and their relationship to associated traits in autism may elucidate shared neural correlates of a range of symptoms in individuals with autism.

Lastly, although research regarding the interaction of motor impairments with the central features of autism is limited, emergent studies in neurodevelopmental disorders is advancing an understanding of the clinical implications of motor symptomology, and thus findings may inform diagnostic measures. Shifting away from the investigational domain however, neuromotor deficits undoubtedly impact on functioning in individuals with autism, thus there exists an important translational component to consider in the context of functional skills, and achieving a repertoire of capacities essential for independence and also social functioning.

The subsequent chapter presents the research study examining APAs in adults diagnosed with autism and IQ-matched neurotypical participants within the framework of the BMLL task.

# *Chapter 2*

## *Anticipatory Postural Adjustments in autism*

*ABSTRACT*

***Objectives**:* The purpose of this preliminary study was to quantify anticipatory postural adjustments (APAs) in adults diagnosed with autism and IQ-matched neurotypical participants.

***Methods:*** *9* participants with a diagnosis of autism and 8 neurotypical participants performed a bimanual load lifting task (BMLL) task, in a seated position, with elbow flexion at 90 degrees and a force sensor secured to the wrist region. A weight resting upon the sensor was unloaded during volitional (unloading produced by the participant's opposing arm) and imposed (produced by the experimenter) conditions. Surface electromyography (sEMG) of the biceps brachii, representing the degree of skeletal muscle activation, was analyzed within the framework of the BMLL.

***Results**:* In the autism group and the neurotypical group, the latency, magnitude and anticipatory response in relation to biceps brachii inhibition was found to not differ significantly. However, group differences emerged in the degree of biceps brachii inhibitory response, wherein the neurotypical participants demonstrated a decreased biceps brachii inhibition within the volitional condition, compared to the autistic group, wherein this reduced biceps brachii inhibition was absent. Also, of relevance, 3 out of the 4 subtests of the Purdue Peg Test were found to be significant in the autistic group thus indicating impaired manual dexterity.

***Conclusions:*** Deficient postural adjustments were not evidenced in the adults with autism, thus indicating an efficient anticipatory adaption of muscle contribution and stabilization performance, preceding the unloading event. Thus, deficient postural adjustments do not appear to contribute to well-established coordination deficits in adult individuals with autism.

## *2.1 Introduction*

*Human movement and postural control*

Human movement, dependent upon the elaborate integration of both cognitive and physical skills, requires observation, generation, execution, and coordination of complex motor patterns. Underlying these processes is postural control, formed through internal representations or sensori-motor programs, which are designed to stabilize joints via control of co-activation of agonists and antagonists during movement (Noback, Ruggiero, Demarest, Strominger, 2005; Umphred, 2007). Specifically, the mechanisms of postural control are seen as an integral element of the neurophysiological basis of diverse, coordinated movement capacities, which in turn, underlies precision in movement performance (Jover et al., 2010).

Coordinated movement however, relies not only on postural control, but requires anticipatory behaviour, which is concerned with predicting the consequences of a planned motor action. This anticipatory capacity is assumed to occur via anticipatory postural adjustments (APAs), representing adaptions in background muscle activity preceeding volitional movement ( Shiratori & Aruin, 2007).

This preliminary study quantifies APAs associated with anticipatory behaviour and spatiotemporal accuracy of coordination in adults diagnosed with autism and IQ-matched neurotypical participants.

*Overview of APAs*

In examining anticipatory behaviour, sensori-motor programs forming the neural basis of skilled motor behaviour, are assumed to be linked to forward model predictors which subserve APAs. According to motor control theories, APAs then formulate estimations of action outcomes (Gowen & Hamilton, 2013). These formulations are then transposed into

action planning to thus maintain postural control and subsequent spatiotemporal accuracy of coordinated movement. From a functional view, APAs, reliant upon feedforward mechanisms that enable the central nervous system to counteract predicted mechanical effects of pertubations (Ng et al., 2011), thus act to minimize disruptions to the body's state of equilibrium. As well as being centrally controlled, APAs rely upon biomechanical parameters of volitional movement, such as movement velocity, (Brunt, Liu, Trimble, Bauer, & Short, 1999; Mochizuki, Ivanova &Garland, 2004), initial and final positions of the body (Aruin & Shiratori, 2003) and also the inertial load of a forthcoming volitional action (Bouisset, 1991).

The development of APAs is characterized by an early emergence, however, a slow maturation ensues throughout childhood. In ongoing development, muscle patterns become more efficient with greater accuracy emerging within the temporal aspects of APAs in regard to unloading events (Schmitz & Assaiante, 2002). In examination of the BMLL task in children at 3-4 years of age stabilisation of the forearm presents, and at 4-6 years of age, children demonstrate a co-contraction pattern of antagonist muscles in the maintainence of stability. Temporal precision of the latency of muscle inhibition, required for refinement of APAs within movement actions, is emergent at 8 years of age, though the temporal qualities are not reflective of the adult level (Schmitz & Assaiante, 2002). Throughout ontogeny, APAs continue to evolve and become more refined through experiential learning and repeated practice (Barlaam et al., 2012a; Witherington et al., 2002). Speculatively, although the development of anticipatory behaviour is principally directed by neurophysiological characteristics and cognitive abilities, associations may exist with motor imagery, potentially linked to the construction of predictive models, as well as processes concerning the coding of anticipatory behaviour in memory, and lastly, diversity in perceptual motor constructs. Later in maturation, modulation of APAs occurs via high-level cognitive processes, of anticipation, attention (Tomita, Fujiwara, Mori, & Sakurai, 2012), and also knowledge of a required response to stimuli, wherein knowledge is accessed prior to stimuli presentation (Jennings, & van der Molen, 2005). Hence, an individual's neurophysiological characteristics, perceptual skills, and cognitive abilities appear to be integral components in the evolution of enhanced anticipatory behaviour.

*APAs analysis*

An analysis of anticipatory behaviour is performed using the BMLL task, as depicted by the actvity of a waiter who lifts a glass from a tray of drinks. The precision of motor coordination to avoid spillage requires postural control via anticipation of a change in the load-bearing arm. The BMLL task specifically consists of unloading the forearm during a volitional movement produced by the participant's opposing arm. This coordinated movement is associated with feed-forward control, and dependent on an accurate representation of the load, and also coordinated movement between the arm initiating the unloading and the forearm position, in minimizing forearm disruptions during the process of unloading. Thus the BMLL allows examination of muscle contribution and kinematics which reflects the functionality of APAs (Jover et al., 2010).

In addition, the quantitiative, spatial, and temporal features of APAs are analyzed via surface electromyography (sEMG) (Pereira, et al., 2014). In particular, postural control mechanisms are delineated via the temporal characteristics of APAs, or the timing of muscle activation. Prior to the onset of action initiation, alteration in postural muscle activation occurs at approximately 100ms; +/- 50ms (Yoshida, Nakazawa, Shimizu, Shimoyama., 2008). During the BMLL task, postural stabilization is assumed to occur, if early inhibition of muscle function occurs within the anticipatory parameter of before +50ms. (Krishnan et al., 2012).

*Dysfunction in APAs*

Variable and imprecise APAs, are proposed to be underpinned by hierarchical motor disruptions, comprising of deficits in multi-sensory integration and processing, which impact on motor execution (Gowen & Hamilton, 2013). Consequences linked to altered APA generation, include impairments in neuromotor strategies and also sequencing of movements. These motor impairments have been found in Parkinson's disease, with dysfunction of the basal ganglia seen as linked to the causation of these impairments. Similarly, these deficits also present in patients with lesions of the primary motor cortex (M1), and supplementary motor area (SMA) (Viallet, 1987). Notably, in patients with lesions of the cerebellum, investigations of APA generation and cerebellar function

revealed preservation of APAs, (Timmann and Horak, 2001), although altered temporal characteristics of APAs were found. Thus, these findings indicate possible differing neural basis underpinning the variable APAs features in these clinical populations. Of note, however, cortical regions do not function in isolation, thus concepts of functional specialization of specific regions of the brain need to be considered within the context of the interactive nature of cortical systems as a whole.

*APAs research in autism*

To date, APAs function in autism has only been examined in children with ASD, thus the features of APAs in adults with autism is unknown. The study by Schmitz, Martineau, Barthélémy, & Assaiante (2003), investigated APAs development in children with autism within a BMLL task, involving measurement of biceps brachii activity via sEMG and also recording of elbow joint angle, to reflect postural stability, during an unloading procedure. The findings from the study reported a deficient postural anticipation, with latencies occurring in both kinematics and muscular events in children with autism compared to neurotypical children. The impaired APAs function in the autistic group was proposed to represent a feedback mode of control in contrast to feedforward mode.

Specifically, Schmitz's study examined 8 children with autism (age range 5.9-10.6, and IQ >70), compared to 16 neurotypical children (age range 4.1-8). No IQ test was reported for neurotypical group, and there was no clear indication that any parameters were matched between the 2 groups. The BMLL task involved a voluntary unloading condition, wherein the right arm performed lifting of the load, which was secured to the left forearm. The left arm however, was positioned in a semi-pronated position, thus this would indicate that the muscle activity wasn't involving pure flexion of the biceps brachii, as the brachioradialis is a strong flexor when the forearm is in midposition between supination and pronation. In fact, when in pronation the brachioradialis is more active during elbow flexion as the biceps brachii is at a mechanical disadvantage. Thus, the measures adopted in the study may not have been capable of yielding a definitive reflection of efficient biceps brachii activation. The study also had a very low number of trials, thus potentially affecting reliability; the total number of trials in the volitional condition was 10 trials and in the imposed unloading condition, 5 trials were performed in total. Additionally, no

testing was performed on the contralateral arm, thus there was no comparison of the effects of the procedure on the dominant (right) arm.

In regard to the analysis of quantitative parameters of APAs, the study focused upon biceps brachii inhibition in relation to latency and also duration of the inhibition response. The latency was measured as the time interval between the onset of unloading and the onset of the reduction of activity, while duration was measured between onset and end of reduction of activity. Thus, both latency and duration of biceps brachii inhibition appears to have been examined at the onset of the unloading event, in contrast to measurement at the commencement of the anticipatory parameter of before +50ms. Hence, the study measures do not appear to take into account the alteration in anticipatory postural muscle activation seen to occur prior to the onset of unloading. Although, in the study it is reported that in the volitional unloading condition, biceps brachii inhibition occurred prior to the onset of unloading in the neurotypical group. Furthermore, the autistic group was reported to show this pattern of activity during unloading, (and thus not preceding unloading) which was assumed to reflect a deficient anticipatory response. Despite the inconsistency regarding the measures in the study, it does appear that APAs alterations were measured within the anticipatory parameter of before +50ms. One further finding in the study refers to the upward deflection of the left arm during unloading. This activity was measured by the potentiometer, and was reported to occur for a shorter duration and to present earlier in the neurotypical group in comparison to the autistic group. However the measurement procedure of the elbow joint angle was not specified.

In sum, the findings in the study reported deficient postural anticipation in autistic children, although the authors highlight that despite this impairment, performance of bimanual coordination is achieved in the autistic group. The examination of bimanual coordination in the study however, appears to be via observation within the BMLL task, and no other apparent neuromotor tests to assess levels of upper limb coordinative function, were performed. The other aforementioned factors within the study that may have impinged on the reliability of the participants responses include the small sample size in conjunction with a wide age range, the lack of clarity in regard to matching of parameters of the 2 groups, the low number of trials performed and the exclusion of testing of the dominant arm, and finally, testing of the forearm in the semi-pronated

position with the biceps brachii at a mechanical disadvantage. Hence, these factors collectively may contribute to problems in the stability of the test scores.

The second study investigated APAs within the framework of the BMLL task in 7 children with autism (age ranges 5.9 -10.6 years, and IQ> 70) in comparison to 7 neurotypical children (age ranges 5.2-9.8), using a similar protocol to that of the Schmitz study (Martineau et al., 2004). In contrast to Schmitz's study, however, potential cortical correlates were measured via electroencephalography (EEG) to determine contribution of central mechanisms to APAs characteristics. Specifically, Martineau's study examined event-related desynchronization (ERD), which has been shown to precede movement onset in adults. The findings reported an absence of ERD prior to onset of movement within the volitional unloading condition in children with autism, which was assumed to reflect deficient anticipation in postural control associated with atypical motor preparation.

As similar to Schmitz's study, the left arm only was measured as the postural arm, which was placed in a supine or semi-pronated position without any specific instruction. The procedure involved trials comprising of 5 unpredictable load-releases, (whereby the experimenter switched off a magnet control to release the load at unpredictable times), followed by 10 lifts in a volitional one-handed condition and 10 lifts in a volitional bimanual condition. The test finished with 5 unpredicted load releases. The numbers of trials excluded within the study were not detailed, and also it is unclear in the study how the onset of lifting was indexed. Furthermore, a single EEG electrode was placed over the M1, which may have limited the efficacy of measurement of cortical responses and additionally may not necessarily reflect responses within this cortical region exclusively ( Ng, Sowman, Brock, & Johnson, 2011). Also, data were band passed filtered for 4 EEG frequency bands of interest: 6-8, 8-10, 10-12, 13-25 Hz, thus potentially contributing to problems with multiple comparisons.

Overall, the study comprised of a small sample size, with a low number of trials, entailing that the data (as shown in the published figures) were extremely noisy. Lastly, the study focused the analysis on the theta frequency range, which is comparative to mu rhythm in adults, and is seen as originating in the somatosensory cortex. Thus the theta ERD in

Martineau's study may not reflect activity within the M1 ( Ng, Sowman, Brock, & Johnson, 2011).

Shifting from the neurocognitive path in advancing scientific research regarding the causation of postural impairments in autism, the effects upon the experience of individuals with autism manifests in the diverse challenges in motor function and associated skills. Of relevance, impaired postural function is believed to impact on the development of coordination skills, spatial and body awareness, social functioning, learning capacities, and also academic skills (MacDonald et al., 2013). To illustrate, in considering the relationship of postural development and learning, both motor patterning and postural control, are seen to preceed prepositional concept learning, such as understanding up and down and left and right, as these skills are firstly learnt within the child's body, prior to the knowledge being translated to other learning domains ( Umphred, 2007 ). Postural and motor development thus may contribute to learning capacities that span physicality, cognitive and behavioural dimensions, therefore conceptualising postural mechanisms in autism, may provide an understanding of the emergence of atypical developmental trajectories in individuals with autism.

*Overview of current APAs study in individuals with autism*

Within this study, spatial, quantitiative and temporal dimensions of APAs of the upper limb, specifically, the biceps brachii, is analysed via sEMG in adults with autism, and IQ-matched controls. Specifically, the temporal characteristics of APAs, utilized to assess the mechanisms of postural control, are typically expected to occur at approximately 100ms; +/- 50ms prior to the onset of action initiation. Thus postural stabilization during the task is assumed to occur if early inhibition of biceps brachii presents within the anticipatory parameter of before +50ms. In the event of inaccuracy of timing of muscle activation sequences reduced forearm postural stabilisation would be expected. Of relevance, recent paradigms of postural control suggest that impaired predictive modeling of muscle force, specifically the timing paramenters in APAs, underlies altered postural control. In bimanually coordinated movement, this predictive impairment is seen to originate in "impaired integration of kinaesthetic and visuomotor feedback concerning the weight of

the load, onset of unloading, and temporal, and spatial coordination between the two arms" (Jover et al., 2010, p. 854).

In addition to analysis via sEMG, examinination of kinematics and muscle contribution, considered to also be an indicator of APA function, is assessed via the BMLL task, wherein the unloading of the forearm during a volitional movement produced by the participant's other arm, requires anticipatory behaviour to compensate for the effects of the unloading. As highlighted, this coordinated movement requires high-level neuromotor coordination, which in turn relies on APA implementation and a series of processes including selection of an optimal motor programme, feed-forward control, accurate representation of the load, (Noback, Ruggiero, Demarest, Strominger, 2005; Umphred, 2007) and synchronous movement between the arm initiating the unloading and the forearm position to ensure reduction of disturbance to the forearm during unloading.

In this current study our hypothesis is that, within the imposed condition the characteristics of APAs will be similar in both the autistic and neurotypical groups. In regard to the volitional condition, we predict the neurotypical group will demonstrate an anticipatory response of biceps brachii inhibition prior to the unloading event. In contrast, the autistic participants in the volitional condition are proposed to have the following APAs features; delayed timing adjustments in biceps brachii inhibition and reactive changes rather than predictive in relation to muscle activity. Overall, these features may reflect a hierarchical motor disruption involving sensori-motor integration, anticipatory behaviour, and motor planning, with a subsequent impact on performance on coordinated movement patterning.

## *2.2 Methodology*

*Participants*

9 adults (3 female and 6 male, 19-36 years) diagnosed with autism, recruited from Autism Spectrum Australia (ASPECT) and Sydney Autism Research website and 8 right-handed neurotypical adults (6 females and 2 males, 19-26 years), recruited from Macquarie

University, participated in the study. Eligibility criteria for inclusion within the study was that participants had to be able to attend the study independently. Thus the ASD participants expectedly fell within the HFA subgroup of ASD. Demographic, ASD symptomology, and IQ results of the 2 groups, are summarized in Table 1. Significant group differences were observed for the effect of age (p=.001) and for presentation of ASD traits across participants (p=.001). The implications of these differences are presented in the discussion section.

| | ***ASD (n=9)*** | | ***Controls (n=8)*** | | | |
|---|---|---|---|---|---|---|
| *Variable* | *Mean* | *SD* | *Mean* | *SD* | *t* | *p* |
| *Age in years* | *27.111* | *5.967* | *20.375* | *0.517* | *3.171* | *0.001* |
| *EHI* | *61.15* | *34.75* | *57.56* | *50.13* | *.452* | *.658* |
| *AQ Score* | *29.555* | *12.521* | *10.181* | *5.723* | *4.123* | *0.001* |
| *WASI VC* | *41.777* | *8.569* | *46.500* | *7.596* | *-1.195* | *0.251* |
| *WASI MR* | *48.777* | *6.996* | *56.125* | *8.838* | *-1.912* | *0.075* |

*Table 1. (Above) Standardized means and standard deviations (SD), t-test and significance scores of demographic, including a measure of handedness, Edinburgh Handedness Inventory (EHI) and ASD symptomology screening measure,The Autism Quotient ( AQ) and IQ measures (WASI-11 Verbal Comprehension (VC) and Matrix Reasoning (MR)) in the ASD group and Control group.*

ASD participants had previously had a diagnosis established by clinical psychologists, and met DSM-4 criteria for ASD. Additionally, autistic traits were evaluated using the Autism Quotient (AQ; Baron-Cohen, Wheelwright, & Skinner, 2001), which provides a continuous and quantitative measure of characteristics associated with autism. The AQ comprises of fifty items with 5 subcategories: social, communicative, attention switching, attention to detail and imagination, posited as representative of characteristics of individuals with autism. The response to various items is via the Likert Scale, varying from strongly disagrees to strongly age. A score above the cut-off number of 32 is assumed to suggest a diagnosis of autism. Within the study, the range of scores was 18 to 39 in the ASD group with 3 participants below the 32 threshold. Of note, a significant difference was found between the 2 groups.

Evaluation of handedness was carried out using the Edinburgh Handedness Inventory (EHI), ( Oldfield, 1971). Right handedness however, was not an inclusion criteria as testing was bilateral. The EHI comprises 10 items, which index hand preference. For each item, participants indicate their hand preference from strong (++), less strong (+), to indifferent (+/+). Responses are recorded into a 5-point Likert scale. In the study, 13 of the participants were right handed, 1 left handed, and 3 ambidextrous according to the inventory. No significant differences were shown between the 2 groups.

In the study, no cognitive inclusion criteria was set, however all participants completed two subtests of the Weschsler Intelligence Scale for Adults (WASI-11), (Wechsler, 2011), which is a standardized measure of verbal and non-verbal abilities and is suitable for ages 6-90 years. There are 4 subtests that contribute to a number of indices of intellectual functioning. For the current study, only the Verbal Comprehension Index (VCI) and Matrix Reasoning (MR) scores are reported. The Verbal comprehension scores and Matrix reasoning scores were used rather than the full IQ score, as full IQ scores encompass executive functioning and extra motor load, and may therefore disadvantage adults with autism by giving a less accurate measure of their full IQ. No significant differences between the 2 groups were found on the 2 subtests.

Participants with a diagnosis of autism also completed the Purdue Pegboard Test, (Yancosek & Howell, 2009), which is a timed physical measure of unimanual and bimanual finger and hand manipulative dexterity for use in neuropsychological assessment to assist in localizing cerebral deficits. The Purdue Pegboard Test was used to examine any possible links between postural control and upper limb coordination. The results from the Purdue Peg Test are summarized in Table 3.

All participants provided informed, written consent to the procedures, in accordance with the Declaration of Helsinki. The Macquarie University Human Research Ethics Committee approved the study.

*Apparatus and Procedures*

Participants performed a BMLL task, (as described by Schmitz, Martineau, Barthélémy, & Assaiante, 2003) comprising of volitional and imposed conditions at the Macquarie University's Action Laboratory. Participants were in a seated position, with their load-bearing arm positioned alongside their trunk, with elbow flexion at 90 degrees and supination of the forearm with the olecranon process only supported upon an armrest. A force sensor mounted on a platform *(12cm x 12cm)* was secured to the load-bearing arm proximal to the wrist joint. Following cleaning of the skin with alcohol wipes, surface electrodes (Brain Products, Gilching, Germany) were attached to the muscle belly of triceps brachii and biceps brachii muscles. A ground electrode was attached to the distal aspect of the forearm, (see Figure 1.).

*Fig. 1. (Above) Graphic representation of BMLL trials showing the position of the apparatus and forearm during both conditions. At the start of the trial, the participant positions the opposite hand near the .750kg weight (the weight is positioned on the force sensor, which is attached to the forearm, proximal to the wrist joint). With an appropriate grip aperture, the weight is then lifted upwards in a direct vertical manner. The procedure is carried out in the same manner for the imposed condition without a prompt for the onset of unloading event.*

Using "Presentation" software, auditory instructions were presented via a monitor positioned at a right angle to the participant's line of sight. Throughout the testing, participants were instructed to fixate ahead to ensure that the lifting action performed by the experimenter was obscured from vision. Compliance with fixation was continuously monitored throughout the experiment.

For the BMLL procedure, participants were given a practice trial, prior to collection of

data. At the onset of the trial, a visual cue 'ready' was projected onto the monitor to prompt participants to prepare for the trial, and a 0.75 kg weight was then placed over the force sensor by the experimenter. Following positioning of the weight, an auditory cue of 'subject lift' or 'experiment lift' followed by a beep was presented to indicate the onset of the unloading procedure. For the voluntary trial, the participant's non- weight bearing hand was positioned near the weight, following the cue of 'subject lift', (with an appropriate grip aperture) and upon the auditory beep, the weight was lifted voluntarily from the sensor. The participant then replaced the weight upon the sensor following the lifting action. For the imposed trials, the experimenter lifted the weight in the same manner, without any prompt of when the event would occur, wherein the timing of the lift occurred randomly within a 10 second time frame. The participant was informed of the ensuing event of the experimenter lifting the weight, prior to commencement of the trials.

A transistor-to -transistor logic pulse, reflecting onset of lifting, is elicited when the weight was lifted from the force sensor, which is then sent to the data acquisition computer during both conditions. In total, 80 trials (2 blocks x 40 trials) were performed in a fixed pseudo-random order per condition with a rest period of 10 seconds between each block. Additional rest periods were provided as needed. The order of the trials was counterbalanced between participants. Bilateral testing was carried out during the testing procedures.

*Data acquisition*

Unloading forces were sampled utilizing a fiber-optic force sensor, which was positioned underneath the 0.75kg weight. EMG activity, recorded from the biceps brachii, which contributes to elbow joint torque of the loaded arm, was collected and sampled at 4kHz, and filtered online between 20 and 500Hz, then amplified (x1000) with a custom-built amplifier, based upon a design reported by Millard, 1992. All preprocessing steps were completed utilizing customized Matlab scripts.

*Data analysis*

EMG data were epoched from 1000ms prior to the unloading event up to 1000ms post-

unloading. The EMG data were then grouped by condition and arm, rectified and then averaged across trials for each participant. EMG modulation during the unloading event was represented in a plot graph showing amplitude against time functions. The onset of inhibition, corresponding to the latency of the initial downward deflection in biceps brachii EMG, was determined via a threshold-crossing algorithm, outlined by DiFabio (1987).

Statistical analysis was performed using a univariate analysis of variance (ANOVA) to assess biceps brachii EMG amplitude in both volitional and imposed conditions across the 2 groups. An independent samples T-Test was then utilized to analyze within-subject effects and between-subjects effects in the biceps brachii EMG amplitude in the 2 conditions. A paired samples t-test also analyzed the effect of condition in both the ASD and control group. A two-tailed significance level was set at $p < .05$ as the standard for significance in all analyses. Statistical analysis was completed with Statistical Package for Social sciences (SPSS: IBM).

## *2.3 Results*

*2.3.1 Purdue Pegboard Test*

| | ***Raw Scores ASD (n=9)*** | | ***Standardized Scores ASD (n=9)*** | | | |
|---|---|---|---|---|---|---|
| *Variable* | *Mean* | *SD* | *Mean* | *SD* | *t* | *P* |
| *Purdue PH* | *14.88* | *2.45* | *-.698* | *1.331* | -1.575 | .154 |
| *Purdue NPH* | *13.55* | *2.32* | *-1.100* | *1.336* | -2.469 | .039 |
| *Purdue BH* | *10.38* | *5.72* | *-1.749* | *1.384* | -3.791 | .005 |
| *Purdue asmb* | *8.33* | *6.84* | *-2.416* | *1.510* | -4.800 | .001 |

*Table 3. (above) Raw and standardized means and standard deviations (SD) of Purdue pegboard subtests comprising of preferred hand (PH), non preferred hand (NPH), both hands (BH), and assembly (asmb) of ASD group.*

*Purdue Pegboard Test Data representing manual dexterity*

The PPT was utilized to ascertain any possible links with postural deficits and impaired coordinative function of the upper limbs, which relates to the hypothesis concerning impaired APA generation and associations with coordinative motor deficits.

The standardized scores of the PPT were derived by calculating z-scores based on the published means and standard deviations for participants in the relevant age groups. PPT analysis involved a one-sample t-test to determine whether participants with ASD had standardized scores significantly below zero. The preferred hand (PH) subtest was non significant (p=.154), however all other subtests were found to be significant; non-preferred hand (NPH,) (p=.039), both hands (BH) (p=.005), and assembly (asmb)(p=.001), thus suggesting relatively distinct impairments in gross motor dexterity of hands, fingers and arms, and fine motor dexterity of fingertips in the ASD group.

*2.3.2.EMG Data*

*Anticipatory Postural Adjustments of 2 groups*

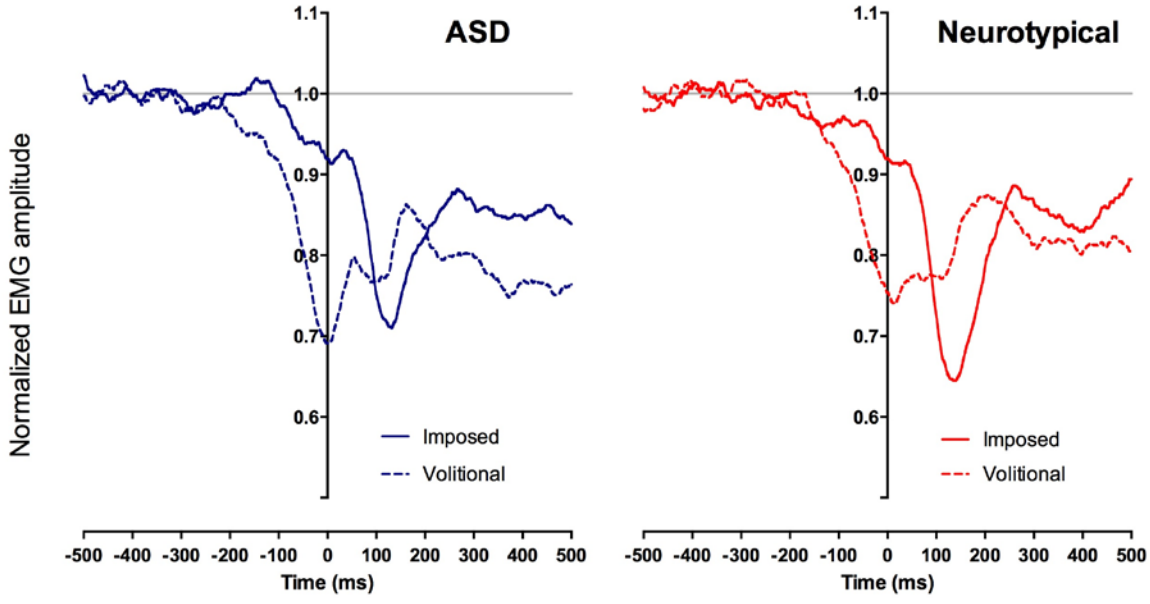


*Figure 2. (above) is a graphical representation of mean EMG amplitude, recorded from biceps brachii inhibition in - 100ms phase prior to unloading as a function of time. Zero (0) represents time when the weight was unloaded from force sensor. The EMG amplitude of biceps brachii inhibition for the 2 groups began to decrease at a latency of approximately -150ms for volitional unloading*

*(volitional)(dashed line). Comparatively, within the 2 groups, biceps brachii inhibition began to decrease only after imposed unloading (imposed)(solid line).*

*a.EMG amplitude data reflecting anticipatory response*

To quantify the anticipatory response, we calculated the mean EMG amplitude of biceps brachii inhibition of both the control group and the ASD group, recorded from the load-bearing arm in the 100ms preceding unloading of the weight from the force sensor (i.e., the area above the curve between -100 and 0 ms) as depicted in figure 2. Utilizing ANOVA, including tests of within-subjects effects of group, arm, and condition, a statistically significant main effect of condition was identified across both groups ($F(1,15)=33.99$, $p<.001$). However, no significant differences were observed in the effect of arm ($F(1,15)= 0.058$, $p=.813$), the effect of group ($F(1,15)=.107$, $p=.728$), and critically, the expected interaction effect of condition and group ($F(1, 15)=.553$, $p=.469$) was not significant. No other interactions approached significance.

As a result of a significant main effect of condition, further analysis was performed to consider the 2 groups independently. A paired samples t-test confirmed the effect of condition in the ASD group, ($t(8)=5.82$, $p< .001$), and the control group, ($t(7)=2.99$, $p= .020$). Overall, both groups showed efficient anticipatory postural adjustments to counterbalance the unloading event, with no evidence of a difference in the amplitude of the anticipatory response between the 2 groups( refer to figure 3.)

*Mean magnitude of anticipatory response*

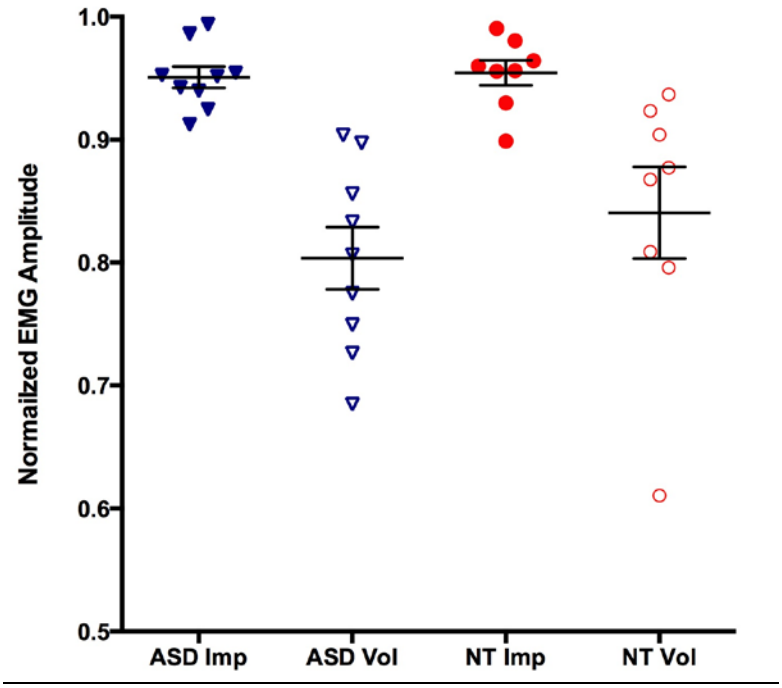


*Figure 3. (above) illustrates mean EMG magnitude of biceps brachii inhibition in the 100ms phase preceding unloading, relative to the baseline (represented by '1.0') in volitional and imposed conditions in the autism and neurotypical groups.*

*c. Mean EMG amplitude of biceps brachii inhibition across both conditions*

Upon visual evaluation of figure 2. which depicts mean EMG amplitude of biceps brachii phase prior to unloading, possible group differences in relation to the extent of the mean amplitude of biceps brachii inhibition across the 2 conditions for all participants is indicated. Specifically, the neurotypical group portrayed a reduced magnitude of the biceps brachii inhibition for volitional condition compared to the imposed condition, thus there appears to be a differentiation in the responses across the 2 conditions. In comparison the autistic group, revealed minimal differentiation of the inhibition amplitude between the 2 conditions, thus indicating responses regardless of condition, were almost undifferentiated in the individuals with autism.

Thus, quantifying the mean anticipatory response in the 100ms region of the inhibition phase for the 2 conditions, was therefore considered (see Figure 4). For each subject, the responses in the volitional condition were averaged across a 100ms time phase, centered on the minima at 7ms (i.e. -43 to 57ms.). For the imposed condition, the time window was centered at 132ms (i.e. 82-182ms).

*EMG inhibitory response averaged across the two groups*

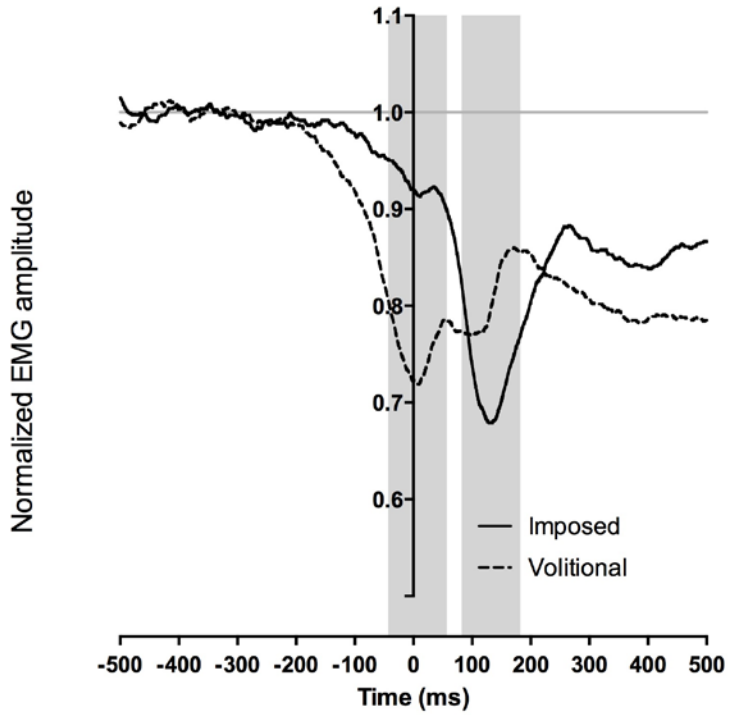


*Figure 4. (above) EMG amplitude inhibitory response averaged across the 2 groups. The shaded area represents the time phase used for analysis of the biceps inhibitory response.*

*EMG amplitude of biceps brachii inhibition across both conditions*

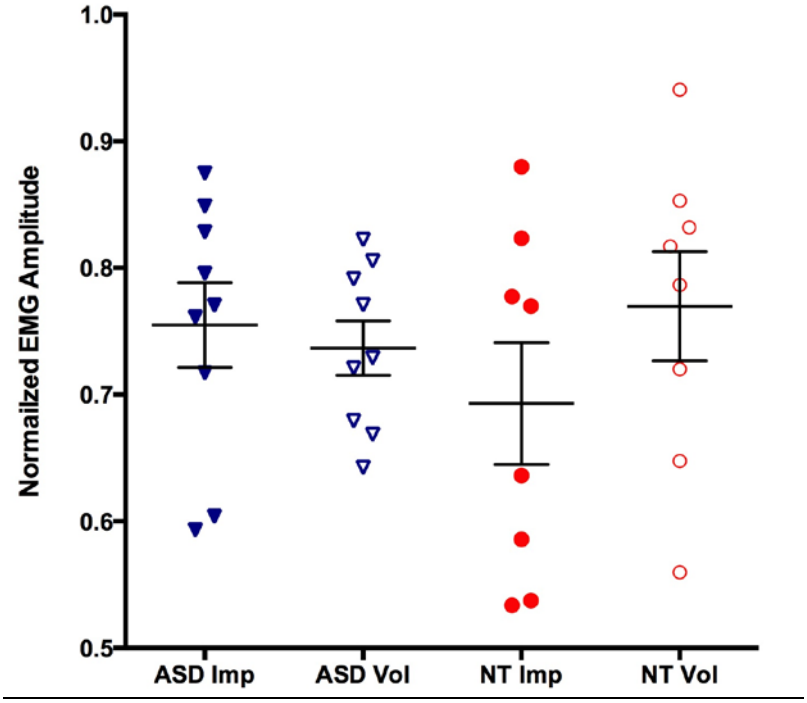


*Figure 5. (above) illustrates the mean EMG amplitude of biceps brachii inhibition across both conditions for all the participants in the 2 groups. The mean normalized EMG amplitude in the imposed condition was calculated from a time phase of 82-182ms, and the mean normalized EMG amplitude in the volitional condition was calculated from a time phase of -43 to 57ms.*

Results of this analysis are shown in Figure 5. No significant differences were identified in the main effect of condition ($F(1,15)=1.48$, $p=.243$), the effect of arm ($F(1,15)= .717$, $p=.410$), or the effect of group ($F(1,15)= .191$, $p=.669$). The observed interaction between condition and group approached significance ( $F(1,15)=3.87$, $p=.068$). No other effects or interactions approached significance, $p>.3$.

Further analysis was also performed to consider the 2 groups independently. A paired samples t-test confirmed that the neurotypical group showed a reduced inhibition

response in the volitional condition, (t (7)=-2.83, p=.026), in comparison to the autistic group which showed no effect of condition, (t(8)=0.47, p= .649).

### *2.4 Discussion*

An efficient motor control system and associated processes are foundational in the performance of skilled, purposeful motor actions, which in turn are essential for functional independence within a range of settings and environments. Integral to motor control, is the control of posture, which depends upon anticipatory behaviour via the generation of APAs.

This preliminary study has highlighted the pervasive nature of motor symptomology in individuals with ASD, with a focus on postural control and coordinated movement behaviour. With recent studies reporting deficient anticipatory behaviour in autism, this study has aimed to quantify APAs, and thus anticipatory behaviour in adults diagnosed with autism compared to IQ-matched controls. Within volitional and imposed conditions, sEMG of the biceps brachii, representing the degree of skeletal muscle activation, was analyzed within the framework of the BMLL to examine the features of APAs in adults with autism.

The BMLL depends on the accuracy of feed-forward models of prospective action to coordinate movement patterns and also maintain postural control, thus requiring a precise sequencing of postural activation and also inhibition. We hypothesized that characteristics of APAs in the adults with ASD, examined within the BMLL task, would comprise of delayed timing adjustments and variability in movement execution. Furthermore we expected a predominance of reactive changes rather than predictive, in terms of muscle action, with subsequent disruption of postural stability. Taken together these features were assumed to reflect a deficient anticipatory behaviour, underpinned by imprecise APAs generation.

Contrary to our predictions, our results showed that the ASD group was

indistinguishable from the control group in terms of anticipatory response, and in the magnitude of muscle inhibition, as observed in both volitional and imposed conditions. Specifically, the comparisons between the ASD group and the control group of the amplitude, magnitude and the mean EMG amplitude of biceps brachii inhibition across both conditions for all participants, did not differ significantly. Hence, the individuals in the ASD group demonstrated a clear predictive adaption of muscle contribution and stabilization performance, preceding an unloading event. Nonetheless, the lack of significance maybe the result of the relatively small sample size, and also due to the heterogeneous nature of ASD.

Although the adults in the ASD group demonstrated an ability to compensate for consequences of the unloading event, there appeared to be less differentiation, i.e. an apparent generalization, in the APA responses across the 2 conditions in the ASD group (in reference to fig.3). This generalized response, was in contrast to that observed in the control group's APAs responses across the 2 conditions. In regard to the control group, a greater variation in APAs responses to the 2 conditions presented as reduced magnitude of inhibition response for the volitional condition, in comparison to a greater magnitude of inhibition response in the imposed condition.

Speculatively, this reduced differentiation or generalization in anticipatory responses in the ASD group, may reflect a similar pattern or strategy of muscle organization for both predicted and unpredicted action events, which in turn may be underpinned by a generalized learning pattern, rather than diversified patterns of motor learning. This lack of differentiation may also represent differences in patterns of motor programming, wherein atypical sensory integration constrains the formation of a range of motor programs, i.e. a more restricted repertoire of motor patterns exist which essentially influences diversity in motor execution, with subsequent impact on coordinated movement.

Also of note, although the results showed no group differences in APA characteristics between the 2 groups, a significant main effect of condition, was confirmed in both groups. This finding thus indicates that APA characteristics clearly varied depending on whether the unloading event was predicted or unpredicted.

Overall, the findings within this present study differ from prior studies of APA generation in autism. In the aforementioned study by Schmitz (2003), deficient postural anticipation was reported, as well as latencies in kinematics and muscular events, which were proposed to be indicative of a feedback mode of control, as opposed to feedforward control. The authors suggest that underlying the deficient APAs response was an impairment in internal representations, as well as deficits in timing parameters. The current study however, differed from the study by Schmitz in a number of aspects, including participant's age and methodology. In Schmitz's study, the sample comprised of children with autism, and neurotypical children in an approximate age range of 4-11 years, thus the difference in results between the current study and the study conducted by Schmitz may be the result of maturational discrepancy, in that the development of APAs is considered to be gradual, with refinement occurring in the later stage of adolescence.

Furthermore, in the study by Schmitz, the methodology differed to the current study, wherein the procedure of the trials was firstly an imposed session of 5 trials, (with an unspecified number of lifts) followed by ten lifts in a volitional session, thus the imposed and volitional trials appear to have a pattern, therefore more predictability exists regarding the unloading event in the imposed condition in the study by Schmitz. Within the current study, a greater number of unloading events were performed in random order between the 2 conditions, thus predictability of the unloading event was reduced. In addition, in Schmitz's study, sEMG analysis of the both latency and duration of inhibition in the biceps brachii, commenced at the onset of the unloading event, as opposed to commencing at the anticipatory parameter of before +50ms, wherein alteration in postural muscle activation is assumed to occur prior to the onset of action initiation.

The second study by Martineau (2004), which examined children with autism, (ages approximately 6 to 11) compared with neurotypical children, used a similar protocol to Schmitz's study. The trials included 5 unpredictable load-releases, with subsequent 10 lifts in a volitional one-handed condition, followed by 10 lifts in a volitional bimanual condition, and concluded with 5 unpredicted load releases. Thus the current study again differed from the study by Martineau in relation to the ages of participants and the methodology, hence the differences in outcomes maybe explained by these factors. In

relation to the findings from the study by Martineau, a reduced ERD was reported in the control group, with an absent ERD in the autistic group, prior to onset of movement, which was assumed to reflect atypical motor preparation, with subsequent effects upon motor programming. However, a single EEG electrode was placed over the primary motor cortex, thus the efficacy of this method in detecting an appropriate response is questionable.

As well as methodological and maturation differences in the current study compared to prior studies of APA generation in autism, inconsistent findings across the studies maybe due to the variable cortical substrates described in individuals across the spectrum of autism. Extensive research of autism has described structural and functional alterations, proposed to be related to motor and postural deficits, in the cerebellum (Becker & Stoodley, 2013), basal ganglia (Hollander, Anagnostou, Chaplin, et al., 2005), thalamus, hippocampus, (Saitoh, Karns, Courchesne, 2001), the SMA (Izawa et al., 2012), the frontal, temporal, parietal lobes, and the corpus collosum (Carper & Courchesne, 2005). Furthermore, in children with autism, altered brain activation, suggesting a dependency on alternative pathways for the performance of movement has also been outlined (Verhoeven et al., 2010). Thus, on a speculative basis, anomalies in cortical structures may contribute to differences in the current study compared to prior studies, wherein autistic individuals may differentially depend on alternate neural recruitment vis-à-vis, compensatory mechanisms to manage the existence of cortical anomalies.

Beyond the analysis of APA responses, importantly, the results from the Purdue Peg Board Test were significant in the majority of the subtests, indicating that the individuals with autism displayed marked impairments in manual dexterity, gross and fine motor skills. Thus, these results provide evidence that the individuals with ASD have deficits in these motor skills within the context of manual and bimanual coordination. On the basis of findings from this study, anticipatory behaviour and associated mechanisms do not appear to explain impaired bimanual coordination in this setting. Hence, differing components of motor control, such as, multi-sensory integration, internal action model formation or internal representations, motor planning and motor execution, need to be examined to provide insights into coordination deficits in individuals with autism. In addition, examining relationships between imitation, praxis, perceptual motor processing,

and the performance of coordination may further elucidate contributory factors in impaired motor function in autism. Lastly, in relation to the neural basis of coordination deficits in autism, the findings from the current study do not appear to implicate the proposed cortical regions subserving APAs, primarily, the primary motor cortex, SMA and basal ganglia. Thus, coordination deficits in individuals in autism maybe better explained by atypicalities in structure and function of the corpus callosum and cerebellum.

***Limitations***

Due to the highly heterogeneous clinical presentation of ASD, and the existence of variability in ASD samples in relation to neural anomalies, an attempt to reduce the effect of heterogeneity upon the study results was made by constraining our sample to high-functioning adults within a specific age range. Furthermore, attempts were made to balance the demographic features of the 2 groups. However, age ranges between the 2 groups showed a significant group difference for the effect of age. The effects of age although do not appear to be of relevance as the participants were adults, and thus maturation was assumed to be stabilized, therefore the expectation is that age would not be a particular confound. Secondly similar patterns of motor activation were observed across the 2 groups, hence suggesting similarities in anticipatory behaviour, despite relative differences in age. Future studies will aim to build further data and progress the methods reported here, with the objective to reproduce these findings in larger samples of adults with ASD, with a closer match in age range.

Being a preliminary pilot study, and the study being conducted in a limited time frame, the sample size obtained was influenced by these constraints. Thus, a further limitation relates to the fact that the study was conducted in a relatively small sample of high functioning adults with autism, representing a sub-group of autism, rather than the spectrum collectively. If however, testing had involved a larger sample size, and also differing subgroups within the autistic spectrum, a significant difference may have emerged. Of note, however, the sample size was adequate to show an APA response in the autistic group, although it is not possible to say whether the APAs responses were

distinct from the control group. Overall, the findings differed from previous studies regarding APAs responses in individuals with autism.

Three of the participants in the ASD group also presented below the cut-off AQ score of 32, however a significant group difference was revealed for presentation of ASD traits across participants thus indicating an accurate representation of the ASD group and control group.

Additionally, the parameters of measurement within this study were limited to EMG amplitude, magnitude and mean EMG amplitude of biceps brachii inhibition across both conditions, therefore studies in the future could quantifiably measure cortical mechanisms involved in anticipatory behaviour in autism. Using differing technologies, such as electroencephalography or transcranial magnetic stimulation may expand research on the neural substrates of anticipatory mechanisms in ASD. Furthermore, measurements could be taken across multiples settings that involve varied perturbations and predictability to delineate how environmental aspects influence neural correlates of postural responses.

In conclusion, the outcomes of this preliminary study did not provide evidence of impairment in APA generation in adult individuals with autism, thus the study findings did not support the hypothesis that deficient APAs may play a contributory role in the the well-established coordination deficits across the spectrum of autism.

*Future research directions*

The systems and mechanisms involved in skilled coordinated motor behaviour require, in addition to postural control, the integration of sensori-motor knowledge in the formulation of motor action, which in turn depends on the intricate relationship of perception and cognition. Thus developing novel approaches to unveil the

neurobiological and neurocognitive mechanisms, which reflect impaired motor function in individuals with autism, is essential.

Furthermore, identifying the relationship of altered movement behaviour and related autistic symptomology is crucial to fully conceptualize autism. Delineating the mechanisms underlying postural and motor control in autism and gaining insights into the relationship between movement behavior and its association with cognition in autism may elucidate central autistic characteristics.

In addition, integrating perspectives to derive new models for postural and motor impairments and to examine developmental effects on the emergence of autistic traits is needed to inform both diagnostic criteria and intervention strategies. In particular, enhancing optimal early development of posture, praxis, imitation and refined motor skills, in conjunction with the development of cognitive capacities within inclusive experiential settings, may contribute to harnessing unique and specialized sensory-perceptual processes and divergent learning skills in individuals with autism. Interventions developed within this vein may thus successfully impact on developmental, learning and behavioural outcomes for individuals with autism.

## *Bibliography*

Adolph, K., & Berger, S. (2006). Motor Development. In Damon, W. & Lerner, R., (Series Ed.), Handbook of Child Psych, Vol 2., 6th Ed, (161-213). Hoboken, Wiley &Sons.

Aziz-Zadeh, L., & Damasio, A. (2008). Embodied semantics for actions: findings from functional brain imaging. *J of Physiol., Paris*, *102*(1-3), 35–9. doi:10.1016/j.jphysparis.2008.03.012

Bachevalier, J., & Loveland, K. a. (2006). The orbitofrontal-amygdala circuit and self-regulation of social-emotional behavior in autism. *Neurosc. and Biobehav. Reviews*, *30*(1), 97–117.

Barlaam, F., Fortin, C., Vaugoyeau, M., Schmitz, C., & Assaiante, C. (2012a). Development of action representation during adolescence as assessed from anticipatory control in a bimanual load-lifting task. *Neurosc.*, *221*, 56–68.

Barlaam, F., Fortin, C., Vaugoyeau, M., Schmitz, C., & Assaiante, C. (2012b). Development of action representation during adolescence as assessed from anticipatory control in a bimanual load-lifting task. *Neurosc.*, *221*, 56–68.

Baron-Cohen, S., Wheelwright, S., & Skinner, R. (2001). The autism-spectrum quotient (AQ): Evidence from Asperger Syndrome/high-functioning autism, males and females, scientists and mathematicians. *J of Autism and Dev Dis.*, 31(1), 5-17.

Becker, E. B. E., & Stoodley, C. J. (2013). *Autism spectrum disorder and the cerebellum. Int. review of neurobiol.*(1st ed., Vol. 113, pp. 1–34). Elsevier Inc.

Behere, A., Shahani, L., Noggle, C. & Dean, R. (2012). *J of Neuropsychiatry and Clin. Neurosc.*, *24*, 87–94.

Behrmann, M., Thomas, C., & Humphreys, K. (2006). Seeing it differently: visual processing in autism. *Trends in Cog. Sc. 10*(6), 258–64.

Ben-Sasson, A., Hen, L., Fluss, R., Cermak, S. a, Engel-Yeger, B., & Gal, E. (2009). A meta-analysis of sensory modulation symptoms in individuals with autism spectrum disorders. *J. of Autism and Dev. Dis.*, *39*(1), 1–11.

Bhat, A. N., Galloway, J. C., & Landa, R. J. (2012). Relation between early motor delay and later communication delay in infants at risk for autism. *Infant Behav Dev*, *35*(4), 838–846.

Bhat, A. N., Landa, R. J., & Galloway, J. C. (2011). Current perspectives on motor functioning in infants, children, and adults with autism spectrum disorders. *Phys Ther*, *91*(7), 1116–1129.

Bhat, A. N., Landa, R. J., & Galloway, J. C. (2011). Current perspectives on motor functioning in infants, children, and adults with autism spectrum disorders. *Phys. Ther.*, *91*(7), 1116–29.

Boucher, J. (2012). Research review: structural language in autistic spectrum disorder - characteristics and causes. *J. of Child Psych. and Psychiatry, and Allied Disciplines*, *53*(3), 219–33.

Braadbaart, L., de Grauw, H., Perrett, D. I., Waiter, G. D., & Williams, J. H. G. (2014). The shared neural basis of empathy and facial imitation accuracy. *NeuroImage*, *84*, 367–75. doi:10.1016/j.neuroimage.2013.08.061

Brunt, D., Liu, S. M., Trimble, M., Bauer, J., & Short, M. (1999). Principles underlying the organization of movement initiation from quiet stance. *Gait & Posture*, *10*(2), 121–8.

Cheldavi, H., Shakerian, S., Nahid, S., & Boshehri, S. (2014). Research in Autism Spectrum Disorders. The effects of balance training intervention on postural control of children with autism spectrum disorder : Role of sensory information. *Res. in Autism Spectrum Disorders*, *8*(1), 8–14.

Chevallier, C., Kohls, G., Troiani, V., Brodkin, E. S., & Schultz, R. T. (2012). The social motivation theory of autism. *Trends in Cog. Sc.*, *16*(4), 231–9.

Coury, D. L., Swedo, S. E., Thurm, A. E., Miller, D. T., Veenstra-VanderWeele, J. M., Carbone, P. S., & Lounds Taylor, J. (2014). Treating the whole person with autism: the proceedings of the Autism Speaks National Autism Conference. *Current Problems in Paed. and Adol. Health Care*, *44*(2), 26–47.

Dawson, M., Mottron, L., Gernsbacher, M. A.,( 2008). Learning in Autism. In J.H. Byrne ( Series Ed.) & H. Roediger ( Vol.Ed), Learning and memory; a comprehensive reference; Cog. Psych, 749-772. NY; Elsevier..

De Jong, M., Punt, M., De Groot, E., Minderaa, R. B., & Hadders-Algra, M. (2011). Minor neurological dysfunction in children with autism spectrum disorder. *Dev. Med. and Child Neuro.*, *53*(7), 641–6.

Dowd, A., Rinehart, N., & McGinley, J. (2010). Motor function in children with autism: Why is this relevant to psychologists? *Clin. Psych.*, *14*(3), 90–96.

Downey, R., & Rapport, M. J. (2012). Motor activity in children with autism: a review of current literature. *Pediatr Phys Ther*, *24*(1), 2–20.

Eapen, V., Crnčec, R., & Walter, A. (2013). Exploring Links between Genotypes, Phenotypes, and Clinical Predictors of Response to Early Intensive Behavioral

Intervention in Autism Spectrum Disorder. *Front. in Human Neurosc.*, *7*(September), 567.

Edwards, L. a. (2014). A meta-analysis of imitation abilities in individuals with autism spectrum disorders. *Autism Res. : Official J of the Int. Society for Autism Res.*, *7*(3), 363–80.

Elliott, D., Hayes, S. J., & Bennett, S. J. (2012). 125 Years of Perceptual-Motor Skill Research. *The Amer. J. of Psych.*, *125*(1), 9–23.

Elsabbagh, M., Divan, G., Koh, Y.-J., Kim, Y. S., Kauchali, S., Marcín, C., … Fombonne, E. (2012). Global prevalence of autism and other pervasive developmental disorders. *Autism Res. : Official J. of the Int.l Soc. for Autism Res.*, *5*(3), 160–79.

Elsabbagh, M., & Johnson, M. H. (2010). Getting answers from babies about autism. *Trends in Cog. Sc. 14*(2), 81–7.

Enticott, P. G., Kennedy, H. a, Rinehart, N. J., Bradshaw, J. L., Tonge, B. J., Daskalakis, Z. J., & Fitzgerald, P. B. (2013). Interpersonal motor resonance in autism spectrum disorder: evidence against a global "mirror system" deficit. *Front. in Human Neurosc. 7*(May), 218.

Estes, A., Shaw, D. W. W., Sparks, B. F., Friedman, S., Giedd, J. N., Dawson, G., … Dager, S. R. (2011). Basal ganglia morphometry and repetitive behavior in young children with autism spectrum disorder. *Autism Res. : Official Jl of the Int. Soc. for Autism Res. 4*(3), 212–20.

Fatemi, S. H., Aldinger, K. A., Ashwood, P., Bauman, M. L., Blaha, C. D., Blatt, G. J., … Welsh, J. P. (2012). Consensus paper: pathological role of the cerebellum in autism. *Cerebellum*, *11*(3), 777–807.

Flanagan, J., Landa, R., Bhat, A., Bauman, M. ( 2012). Head lag in infants at risk for autism; a preliminary study. *Amer. Journal of Occupational Ther.* 66.5, 577

Forti, S., Valli, A., Perego, P., Nobile, M., Crippa, A., & Molteni, M. (2011). Motor planning and control in autism. A kinematic analysis of preschool children. *Res. in Autism Spectrum Disorders*, *5*(2), 834–842.

Fournier, K., Hass, C., Naik, S., Lodha, N., & Cauraugh, J. (2010). Motor coordination in autism spectrum disorders: a synthesis and meta-analysis. *J.l of Autism and Dev. Dis. 40*(10), 1227–40.

Fournier, K., Amon, K., Amano., Radonich, K., Bleser, T., & Hass, C., (2014). Decreased dynamical complexity during quiet stance in children with autism spectrum disorders. *Gait &Posture,* 39, 420-423

Funabiki, Y., Murai, T., & Toichi, M. (2012). Cortical activation during attention to sound in autism spectrum disorders. *Research in Dev. Dis., 33*(2), 518–24. 6

Gabis, L. V, & Pomeroy, J. (2014). An etiologic classification of autism spectrum disorders. *The Israel Med. Assoc. Journ. : IMAJ*, *16*(5), 295–8.

Geschwind, D. H. (2011). Genetics of autism spectrum disorders. *Trends in Cog. Sc., 15*(9), 409–16.

Gooijers, J., & Swinnen, S. P. (2014a). Interactions between brain structure and behavior: the corpus callosum and bimanual coordination. *Neurosc. and Biobehav. Rev.*, *43*, 1–19.

Gooijers, J., & Swinnen, S. P. (2014b). Interactions between brain structure and behavior: the corpus callosum and bimanual coordination. *Neurosc. and Biobehav. Rev.*, *43*, 1–19.

Gowen, E., & Hamilton, A. (2013). Motor abilities in autism: a review using a computational context. *J. of Autism and Dev.l Dis. 43*(2), 323–44.

Happé, F., & Frith, U. (2014). Annual Research Review: Towards a developmental neuroscience of atypical social cognition. *J of Child Psych. and Psychiatry*, *55*(6), 553–577.

Haswell, C. C., Izawa, J., & Dowell, L. R. (2009). Representation of internal models of action in the autistic brain, *Nat. Neurosc.*, *12*(8), 970–972.

Hollocks, M. J., Jones, C. R. G., Pickles, A., Baird, G., Happé, F., Charman, T., & Simonoff, E. (2014). The association between social cognition and executive functioning and symptoms of anxiety and depression in adolescents with autism spectrum disorders. *Autism Res. : Official J of the Int. Soc. for Autism Res., 7*(2), 216–28.

Hoshi, E., & Tanji, J. (2004). Differential roles of neuronal activity in the supplementary and presupplementary motor areas: from information retrieval to motor planning and execution. *J. of Neurophysiol. 92*(6), 3482–99.

Isenhower, R. W., Marsh, K. L., Richardson, M. J., Helt, M., Schmidt, R. C., & Fein, D. (2012). Rhythmic bimanual coordination is impaired in young children with autism spectrum disorder. *Res. in Autism Spectrum Disorders*, *6*(1), 25–31.

Izawa, J., Pekny, S. E., Marko, M. K., Haswell, C. C., Shadmehr, R., & Mostofsky, S. H. (2012). Motor learning relies on integrated sensory inputs in ADHD, but over-selectively on proprioception in autism spectrum conditions. *Autism Res*, *5*(2), 124–136.

Jasmin, E., Couture, M., McKinley, P., Reid, G., Fombonne, E., & Gisel, E. (2009). Sensori-motor and daily living skills of preschool children with autism spectrum disorders. *J. of Autism and Dev. Dis.,s*, *39*(2), 231–41.

Jennings, J, & van der Molen, M. (2005). Preparation for Speeded Action as a Psychophysiological Concept. *Psychol. Bulletin*, *131*(3), 434–459.

Jeste, S. S., & Geschwind, D. H. (2014). Disentangling the heterogeneity of autism spectrum disorder through genetic findings. *Nature Rev., Neuro. 10*(2), 74–81.

Johnson, B. P., Phillips, J. G., Papadopoulos, N., Fielding, J., Tonge, B., & Rinehart, N. J. (2013). Understanding macrographia in children with autism spectrum disorders. *Res Dev Disabil*, *34*(9), 2917–2926.

Jover, M., Schmitz, C., Centelles, L., Chabrol, B., & Assaiante, C. (2010). Anticipatory postural adjustments in a bimanual load-lifting task in children with developmental coordination disorder. *Dev. Med. and Child Neuro.*, *52*(9), 850–5.

Kaiser, M. D., Delmolino, L., Tanaka, J. W., & Shiffrar, M. (2010). Comparison of visual sensitivity to human and object motion in autism spectrum disorder. *Autism Research : Official J. of the Int. Soc. for Autism Res.*, *3*(4), 191–5.

Kana, R. K., Libero, L. E., & Moore, M. S. (2011). Disrupted cortical connectivity theory as an explanatory model for autism spectrum disorders. *Physics of Life Rev.*, *8*(4), 410–37.

Katsyri.J., Saalasti, S., Tiippana, K., Wendt, L. Von, & Sams, M. (2008). Impaired recognition of facial emotions from low-spatial frequencies in Asperger syndrome, *Neuropsych*. *46*, 1888–1897.

Klin, A., Jones, W., Schultz, R., & Volkmar, F. (2003). The enactive mind, or from actions to cognition: lessons from autism. *Phil. Transactions of the Royal Soc. of Lon. Series B, Biol. Sc.*, *358*(1430), 345–60.

Klintwall, L., Holm, A., Eriksson, M., Carlsson, L. H., Olsson, M. B., Hedvall, A., … Fernell, E. (2011). Sensory abnormalities in autism. A brief report. *Research in Dev. Dis.*, *32*(2), 795–800.

Kopp, S., Beckung, E., & Gillberg, C. (2010). Developmental coordination disorder and other motor control problems in girls with autism spectrum disorder and/or attention-deficit/hyperactivity disorder. *Res Dev Disabil*, *31*(2), 350–361.

Krishnan, V., Latash, M. L., & Aruin, A. S. (2012). Early and late components of feed-forward postural adjustments to predictable perturbations. *Clin. Neurophysiol. : Official J. of the Int. Fed.of Clin. Neurophysiol. 123*(5), 1016–26.

Lai, M.-C., Lombardo, M. V, & Baron-Cohen, S. (2014a). Autism. *Lancet*, *383*(9920), 896–910.

Lai, M.-C., Lombardo, M. V, & Baron-Cohen, S. (2014b). Autism. *Lancet*, *383*(9920), 896–910.

Lane, A., Harpster, K., & Heathcock, J. (2012). Motor characteristics of young children referred for possible autism spectrum disorder. *Pediatr Phys Ther*, *24*(1), 21–29.

Leek, E. C., & Johnston, S. J. (2009). Functional specialization in the supplementary motor complex. *Nature Rev. Neurosc. 10*(1), 78.

Lenroot, R. K., & Yeung, P. K. (2013). Heterogeneity within Autism Spectrum Disorders: What have We Learned from Neuroimaging Studies? *Front. in Human Neurosc. 7*(October), 733.

Linkenauger, S., Lerner, M. D., Ramenzoni, V. C., & Proffitt, D. R. (2012). A perceptual-motor deficit predicts social and communicative impairments in individuals with autism spectrum disorders. *Autism Res. : Official J. of the Int. Soc. for Autism Res.5*(5), 352–62.

Liu, T. (2013). Sensory Processing and Motor Skill Performance in Elementary School Children With Autism Spectrum Disorder 1. *Percept. and Motor Skills*, *116*(1), 197–209.

Lombardo, M. V, & Baron-Cohen, S. (2011). The role of the self in mindblindness in autism. *Consciousness and Cog.*, *20*(1), 130–40.

Lombardo, M. V, Chakrabarti, B., Bullmore, E. T., & Baron-Cohen, S. (2011). Specialization of right temporo-parietal junction for mentalizing and its relation to social impairments in autism. *NeuroImage*, *56*(3), 1832–8.

Lombardo, M. V, Chakrabarti, B., Bullmore, E. T., Sadek, S. A., Pasco, G., Wheelwright, S. J., … Baron-Cohen, S. (2010). Atypical neural self-representation in autism. *Brain*, *133*(Pt 2).

Lomond, K. V, Henry, S. M., Jacobs, J. V, Hitt, J. R., Horak, F. B., Cohen, R. G., … DeSarno, M. J. (2013). Protocol to assess the neurophysiology associated with multi-segmental postural coordination. *Physiol Meas*, *34*(10), N97–105.

MacDonald, M., Lord, C., & Ulrich, D. (2013). The relationship of motor skills and adaptive behavior skills in young children with autism spectrum disorders. *Res. in Autism Spectrum Disorders*, *7*(11), 1383–1390.

Macdonald, M, Lord, C, & Ulrich, D. (2014). Motor skills and calibrated autism severity in young children with autism spectrum disorder. *Adapt Phys Activ Q*, *31*(2), 95–105.

MacNeil, L. K., & Mostofsky, S. H. (2012). Specificity of dyspraxia in children with autism. *Neuropsychology*, *26*(2), 165–71. doi:10.1037/a0026955

Mannion, A., & Leader, G. (2013). Comorbidity in autism spectrum disorder: A literature review. *Research in Autism Spectrum Disorders*, *7*(12), 1595–1616.

Mari, M., Castiello, U., Marks, D., Marraffa, C., & Prior, M. (2003). The reach-to-grasp movement in children with autism spectrum disorder. *Phil. Transactions of the Royal Soc. of Lon. Series B, Biological Sciences*, *358*(1430), 393–403.

Martineau, J., Schmitz, C., Assaiante, C., Blanc, R., & Barthélémy, C. (2004). Impairment of a cortical event-related desynchronisation during a bimanual load-lifting task in children with autistic disorder. *Neurosc. Letters*, *367*(3), 298–303.

Matson, J. L., & Jang, J. (2014). Conceptualizing skills that are most critical in diagnosing autism. *Research in Autism Spectrum Disorders*, *8*(8), 968–973.

Matson, J. L., Kozlowski, A. M., & Matson, M. M. (2012). Speech deficits in persons with autism: Etiology and symptom presentation. *Res. in Autism Spectrum Disorders*, *6*(2), 573–577.

Memari, A. H., Ghanouni, P., Shayestehfar, M., Ziaee, V., & Moshayedi, P. (2014). Effects of visual search vs. auditory tasks on postural control in children with autism spectrum disorder. *Gait & Posture*, *39*(1), 229–34.

Mohapatra, S., Krishnan, V., & Aruin, A. S. (2012). Postural control in response to an external perturbation: effect of altered proprioceptive information. *Exp. Brain Res.*, *217*(2), 197–208.

Molloy, C., Dietrich, K., Bhattacharya, A., (2003). Postural stability in children with autism spectrum disorder. *J of Autism and Dev Dis*., 33(6), 643-652.

Monno, a, Chardenon, a, Temprado, J. J., Zanone, P. G., & Laurent, M. (2000). Effects of attention on phase transitions between bimanual coordination patterns: a behavioral and cost analysis in humans. *Neurosc. Letters*, *283*(2), 93–6.

Moseley, R. L., Mohr, B., Lombardo, M. V, Baron-Cohen, S., Hauk, O., & Pulvermüller, F. (2013). Brain and behavioral correlates of action semantic deficits in autism. *Front. in Human Neurosc.*, *7*(Nov.), 725.

Mostofsky, S. H., & Ewen, J. B. (2011). Altered connectivity and action model formation in autism is autism. *Neurosc. 17*(4), 437–448.

Murdoch, J. D., & State, M. W. (2013). Recent developments in the genetics of autism spectrum disorders. *Current Opinion in Genetics & Dev. 23*(3), 310–5.

Nachev, P., Kennard, C., & Husain, M. (2008). Functional role of the supplementary and pre-supplementary motor areas. *Nature Rev. Neurosc., 9*(11), 856–69. 8

Nayate, A., Bradshaw, J., & Rinehart, N. (2005). Autism and Asperger's disorder: Are they movement disorders involving the cerebellum and/or basal ganglia?, *Brain Res. Bulletin.*, *67*(4), 327–334.

Nebel, M. B., Joel, S. E., Muschelli, J., Barber, A. D., Caffo, B. S., Pekar, J. J., & Mostofsky, S. H. (2014). Disruption of functional organization within the primary motor cortex in children with autism. *Human Br. Mapping*, *35*(2), 567–80.

Ng, T. H., Sowman, P. F., Brock, J., & Johnson, B. W. (2011). Premovement brain activity in a bimanual load-lifting task. *Exp Brain Res, 208*(2), 189–201.

Nguyen-Vu, T. D. B., Kimpo, R. R., Rinaldi, J. M., Kohli, A., Zeng, H., Deisseroth, K., & Raymond, J. L. (2013). Cerebellar Purkinje cell activity drives motor learning. *Nature Neurosc.*, *16*(12), 1734–6.

Nickel, L. R., Thatcher, A. R., Keller, F., Wozniak, R. H., & Iverson, J. M. (2013). Posture Development in Infants at Heightened vs. Low Risk for Autism Spectrum Disorders. *Infancy*, *18*(5), 639–661.

Oldfield, C., (1971). The assessment and analysis of handedness. The Edinburgh Hand Inventory. *Neuropsych.* (9), 97-113.

Ozonoff, S., Young, G. S., Belding, A., Hill, M., Hill, A., Hutman, T., … Iosif, A.-M. (2014). The broader autism phenotype in infancy: when does it emerge? *Journal of the American Academy of Child and Adolescent Psychiatry*, *53*(4), 398–407.e2. doi:10.1016/j.jaac.2013.12.020

Ozonoff, S., Young, G. S., Goldring, S., Greiss-Hess, L., Herrera, A. M., Steele, J., … Rogers, S. J. (2008). Gross motor development, movement abnormalities, and early identification of autism. *J of Autism and Dev.l Dis. 38*(4), 644–56.

Parellada, M., Penzol, M. J., Pina, L., Moreno, C., González-Vioque, E., Zalsman, G., & Arango, C. (2014). The neurobiology of autism spectrum disorders. *European Psychiatry : The J of the Assoc. of Euro. Psychiatrists*, *29*(1), 11–9.

Pelphrey, K. a, Shultz, S., Hudac, C. M., & Vander Wyk, B. C. (2011). Research review: Constraining heterogeneity: the social brain and its development in autism spectrum disorder. *J of Child Psych. and Psychiatry, and Allied Discip.*, *52*(6), 631–44.

Piek, J., Gasson, N., & Summers, J. (2008). Motor control and coordination across the lifespan. *Human Movm. Sc.*, *27*(5), 665–7.

Plomin, DeFries, McClearn, &Mc G. (2008). *Behav. genetics(2008)* (5th Ed.). NY: Worth Publishers, NY.

Procacci, N. M., & Stanford, T. R. (2013). The impact of perceptual, cognitive and motor factors on bimanual coordination. *Psychological Research*, *77*(6), 794–807.

Puzzo, I., Cooper, N. R., Vetter, P., & Russo, R. (2010). EEG activation differences in the pre-motor cortex and supplementary motor area between normal individuals with high and low traits of autism. *Brain Res.*, *1342*(2008), 104–10.

Raznahan, A., Wallace, G. L., Antezana, L., Greenstein, D., Lenroot, R., Thurm, A., … Giedd, J. N. (2013). Compared to what? Early brain overgrowth in autism and the perils of population norms. *Biol. Psychiatry*, *74*(8), 563–75.

Rinehart, N. J., Bellgrove, M. a, Tonge, B. J., Brereton, A. V, Howells-Rankin, D., & Bradshaw, J. L. (2006). An examination of movement kinematics in young people with high-functioning autism and Asperger's disorder: further evidence for a motor planning deficit. *J of Autism and Dev. Dis.*, *36*(6), 757–67.

Rinehart, N., & McGinley, J. (2010). Is motor dysfunction core to autism spectrum disorder? *Dev Med Child Neurol*, *52*(8), 697.

Rizzolatti, G., Fogassi, L., & Gallese, V. (2001). Neurophysiolal mechanisms underlying the understanding of imitation of action, Nature Rev., *Neurosc., (2), 661-670*

Rothwell, J. C. (2012). Overview of neurophysiology of movement control. *Clin.Neuro. and Neurosurg.*, *114*(5), 432–5.

Ryland, H. K., Hysing, M., Posserud, M.-B., Gillberg, C., & Lundervold, A. J. (2014). Autistic features in school age children: IQ and gender effects in a population-based cohort. *Res. in Autism Spectrum Disorders*, *8*(3), 266–274.

Santos, M. J., Kanekar, N., & Aruin, A. S. (2010). The role of anticipatory postural adjustments in compensatory control of posture: 1. Electromyographic analysis. *J. of Electromyog. and Kinesiol.: Official J.of the Int. Society of Electrophysiol. Kinesiol. 20*(3), 388–97.

Schmitz, C., & Assaiante, C. (2002). Developmental sequence in the acquisition of anticipation during a new co-ordination in a bimanual load-lifting task in children. *Neurosc. Letters*, *330*(3), 215–8.

Schmitz, C., Martineau, J., Barthélémy, C., & Assaiante, C. (2003). Motor control and children with autism: deficit of anticipatory function? *Neurosc. Letters*, *348*(1), 17–20.

Shibasaki, H. (2012). Cortical activities associated with voluntary movements and involuntary movements. *Clinical Neurophysiol. : Official J. of the Int. Fed. of Clin. Neurophysiol., 123*(2), 229–43.

Stanley-Cary, C., Rinehart, N., Tonge, B., White, O., & Fielding, J. (2011). Greater disruption to control of voluntary saccades in autistic disorder than Asperger's disorder: evidence for greater cerebellar involvement in autism? *Cerebellum (Lon., Eng.)*, *10*(1), 70–80.

Stewart, H. J., McIntosh, R. D., & Williams, J. H. G. (2013). A specific deficit of imitation in autism spectrum disorder. *Autism Res. : Official J.l of the Int. Soc. for Autism Res.*, *6*(6), 522–30.

Sudarov, A. (2013). Defining the role of cerebellar Purkinje cells in autism spectrum disorders. *Cerebellum (Lon., Eng.)*, *12*(6), 950–5.

Tanji, J. (1994). Review article. The supplementary motor area in the cerebral cortex, Neurosc. Res., 19(3), 251-268.

Teitelbaum, P., Teiltebaum, O., Nye, J., Fryman, J., & Maurer, R. (1998). Movement analysis in infancy may be useful for early diagnosis. *Psych. 95*(November), 13982–13987.

Tomita, H., Fujiwara, K., Mori, E., & Sakurai, A. (2012). Effects of anticipation certainty on preparatory brain activity and anticipatory postural adjustments associated with voluntary unilateral arm movement while standing. *Hum Mov Sci*, *31*(3), 578–591.

Tomita, H., Fujiwara, K., Mori, E., & Sakurai, A. (2012). Effects of anticipation certainty on preparatory brain activity and anticipatory postural adjustments associated with voluntary unilateral arm movement while standing. *Human Movm. Sc., 31*(3), 578–91.

Travers, B. G., Powell, P. S., Klinger, L. G., & Klinger, M. R. (2013). Motor difficulties in autism spectrum disorder: linking symptom severity and postural stability. *J of Autism and Dev. Dis., 43*(7), 1568–83.

Uddin, L. Q. (2011). The self in autism: an emerging view from neuroimaging. *Neurocase, 17*(3), 201–8.

Van Buijsen, M., Hendriks, A., Ketelaars, M., & Verhoeven, L. (2011). Assessment of theory of mind in children with communication disorders: role of presentation mode. *Res. in Dev.l Dis. 32*(3), 1038–45.

Verhoeven, J. S., De Cock, P., Lagae, L., & Sunaert, S. (2010). Neuroimaging of autism. *Neuroradiol., 52*(1), 3–14.

Vissers, M. E., Cohen, M. X., & Geurts, H. M. (2012). Brain connectivity and high functioning autism: a promising path of research that needs refined models, methodological convergence, and stronger behavioral links. *Neurosc. and Biobehav. Rev., 36*(1), 604–25.

Vivanti, G., & Rogers, S. J. (2014). Autism and the mirror neuron system: insights from learning and teaching. *Phil.l Transactions of the Royal Soc. of Lon.. Series B, Biol.Sc., 369*(1644), 20130184.

Wechsler, D. (2011). Wechsler Abbreviated Scale of Intelligence, Second Edition (WASI-II*). J of Psychoed. Assessment,* 31(3) 337–341.

Wilson, T. W., Kurz, M. J., & Arpin, D. J. (2014). Functional specialization within the supplementary motor area: a fNIRS study of bimanual coordination. *Neuroimage*, *85 Pt 1*, 445–450.

Wilson, T. W., Kurz, M. J., & Arpin, D. J. (2014). Functional specialization within the supplementary motor area: a fNIRS study of bimanual coordination. *NeuroImage*, *85 Pt 1*, 445–50.

Witherington, D. C., Hofsten, C., Rosander, K., Robinette, A., Woollacott, M. H., & Bertenthal, B. I. (2002). The Development of Anticipatory Postural Adjustments in Infancy. *Infancy*, *3*(4), 495–517.

Yancosek & Howell. (2009). A Narrative Review of Dexterity assessments. *J of Hand Therapy.*(11), 258-270.

Yoshida S., Kakazawa, K., Shimizu, E., Shimoyama, I. (2008) Anticipatory postural adjustments modify the movement-related potentials of upper extremity voluntary movement. *Gait Posture*, 27(1); 97-102.

Zanone, P. G., Monno, a, Temprado, J. J., & Laurent, M. (2001). Shared dynamics of attentional cost and pattern stability. *Human Movmt Sc.e 20*(6), 765–89.

Zwickel, J., White, S. J., Coniston, D., Senju, A., & Frith, U. (2011). Exploring the building blocks of social cognition: spontaneous agency perception and visual perspective taking in autism. *Social Cognitive and Affective Neurosc.*, *6*(5), 564–71.