J Autism Dev Disord (2010) 40:1227–1240
DOI 10.1007/s10803-010-0981-3

ORIGINAL PAPER

Motor Coordination in Autism Spectrum Disorders: A Synthesis and Meta-Analysis

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Published online: 2 March 2010

Abstract Are motor coordination deficits an underlying cardinal feature of Autism Spectrum Disorders (ASD)? Database searches identified 83 ASD studies focused on motor coordination, arm movements, gait, or postural stability deficits. Data extraction involved between-group comparisons for ASD and typically developing controls ($N = 51$). Rigorous meta-analysis techniques including random effects models, forest and funnel plots, I^2, publication bias, fail-safe analysis, and moderator variable analyses determined a significant standardized mean difference effect equal to 1.20 (SE = 0.144; $p < 0.0001$; $Z = 10.49$). This large effect indicated substantial motor coordination deficits in the ASD groups across a wide range of behaviors. The current overall findings portray motor coordination deficits as pervasive across diagnoses, thus, a cardinal feature of ASD.

Keywords ASD · Motor coordination and impairments · Meta-analysis

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Introduction

Autism Spectrum Disorders (ASD) is an inclusive term for a group of neurodevelopmental disorders sharing similar impairments in communication, reciprocal social interaction, and restricted, repetitive behavior. While similar in nature, ASD includes the following distinct diagnoses: autism, Asperger's Syndrome, and Pervasive Developmental Disorder-Not Otherwise Specified (DSM-IV 2000; Tanguay et al. 1998). Recent epidemiological studies provide prevalence estimates in the 60–70/10,000 range, making ASD one of the most frequently observed childhood neurodevelopmental disorders (Fombonne 2009). Although current improvements in diagnostic criteria and refined methodologies may be contributors, the prevalence appears to have increased in recent surveys (Bertoglio and Hendren 2009; Fombonne 2009; Lenoir et al. 2009). Given the frequency reports, not surprisingly, both the lay and scientific communities have rapidly increased their attention to the diagnostic and cardinal features of ASD.

One ASD associated feature requiring more elucidation is disturbances in motor behavior. The literature focusing on gross motor behavior and development in ASD is plagued by inconsistent findings. Early views stressed that children with ASD may have similar motor development (Hallett et al. 1993; Mayes and Calhoun 2003) or perhaps even more advanced motor skills than their peers (Johnson and Myers 2007; Rimland 1964). However, more frequently reported, ASD is associated with greater clumsiness, motor coordination abnormalities, postural instability, and poor performance on standardized tests of motor functioning (Bauman 1992; Ghaziuddin and Butler 1998; Jones and Prior 1985; Kohen-Raz et al. 1992; Molloy et al. 2003; Rapin 1997; Rogers et al. 1996; Vilensky et al. 1981). Further complicating our understanding of the underlying motor features is

that several studies failed to detect differences between children with ASD and those with learning disabilities or mental retardation (Morin and Reid 1985), general developmental delay (Provost et al. 2007b), and language disorders (Noterdaeme et al. 2002) across reflexive, intentional, fine and gross motor tasks. These observations challenge whether disturbed motor performances in ASD are because of alterations in the motor circuits, gross brain dysfunction, or a behavioral byproduct of the interaction between motor function and other core features of ASD. Thus, while these cross-sectional studies provide critical information regarding the types of motor impairments seen in ASD, the specific patterns and sources of motor deficits in this population remain unclear (Noterdaeme et al. 2002).

Other approaches to elucidating motor components of ASD include neural signaling. Abnormal transmission in the serotonergic, dopaminergic, and GABAergic systems, frequently observed in ASD, may potentially affect motor performance (Cook et al. 1997; DeLorey et al. 1998; Nelson et al. 2001). Further, imaging studies have identified significant anomalies within seminal structures controlling motor behavior in individuals with ASD. Indeed, structural imaging studies suggest that individuals with ASD have larger total brain, cerebellar and caudate nucleus volumes; however, the area of the corpus callosum is reduced (for recent reviews see: Hrdlicka 2008; Stanfield et al. 2008). Functional MRI studies have also identified differential activation in brain areas related to motor performances in children with ASD, suggesting a reliance on alternative pathways (Verhoeven et al. 2010). Thus, there appears to be neurobiological underpinning for the clinically observed motor deficits in ASD.

Novel attempts to relate motor impairments in infancy to the onset characteristics of ASD have produced intriguing findings (Teitelbaum et al. 1998). Indeed, several related studies in which motor behavior was evaluated using home videos of children later diagnosed with ASD compared to typically developing children demonstrated motor differences within the first 2 years of age (Adrien et al. 1993; Baranek 1999; Teitelbaum et al. 2004). Though, Ozonoff et al. (2007) failed to replicate these findings. Taken together, this evidence suggests that motor deficits may be present even before communicative or social deficits, implying that impaired motor behavior may underlie an apparent ASD core characteristic (Leary and Hill 1996; Nayate et al. 2005). Certainly, impaired perceptual-motor difficulties can exacerbate other core symptoms by limiting interaction with the physical and social world during critical developmental periods.

Consequently, the delayed onset of motor capabilities and coordination deficits with a distinct association to ASD are of fundamental importance. However, the literature is overflowing with conflicting results, methodological insufficiencies, and highly variable ASD participants and comparison groups across studies. Further, observed results may be biased by the influence of moderating variables such as age and intelligence quotient. Each of these concerns severely obscures our understanding of motor impairments in this population. Thus, an appealing alternative approach that aptly integrates the varied literature and findings is a robust, systematic review and meta-analysis. Conducting a meta-analysis on ASD is an objective and quantitative technique for summarizing the presence of motor control impairments and determining summary effect sizes as well as gaining fundamental insight. Therefore, using the meta-analytic technique, we asked two critical questions:

(1) Do motor control capabilities and/or impairments distinguish children and adults with ASD when compared to neurologically, typically developing normal age-matched controls?
(2) Do upper or lower extremities motor control impairments distinguish children and adults within ASD?

Methods

Study Inclusion and Exclusion Criteria

Conducting an exhaustive search for ASD studies began with three computerized databases (1980–2009): (a) PubMed, (b) ISI's Web of Knowledge, and (c) Cochrane Database of Systematic Reviews. Ten key words and phrases dictated our search: autism, Autism Spectrum Disorders, motor impairment, coordination, balance, posture control system, gait kinematics, gait kinetics, neuromotor deficits, and arm movements. Additional searches involved examining reference lists of retrieved articles. Casting broad selection criteria and not excluding any quantitative study are consistent with recommendations (Rosenthal 1995). Thus, our initial search identified 83 records (all full-length studies: 81 published and two unpublished) that discussed ASD in conjunction with human motor coordination, motor impairment, arm movements, gait, or postural stability.

Four predetermined inclusion/exclusion criteria follow:

1. The first inclusion criterion involved quantitative evaluations on motor coordination, motor impairment, arm movement, gait, or postural stability. Studies that did not meet this criterion included 17 literature reviews (Bugalho et al. 2006; Damasio and Maurer 1978; Fuentes and Bastian 2007; Gillberg 2003; Gillberg and Kadesjo 2003; Jones and Prior 1985; Leary and Hill 1996; Macintosh and Dissanayake 2004; McLaughlin-Cheng 1998; Ming et al. 2007; Nayate et al. 2005; Piek and Dyck 2004; Rinehart et al. 2002; Sugden 2007;

Trevarthen 2000; Uhlhaas and Singer 2006; Wann 2007) and two descriptive studies (Newell et al. 1999; Teitelbaum et al. 1998). Sixty-four of the original 83 studies conducted quantitative evaluations.

2. A second inclusion criterion was relevance to our specific questions. Ten studies were discarded because of lack of relevance to our questions focusing on ASD, motor coordination, arm movements, gait, and postural stability (Accardo et al. 1992; Campbell et al. 1990; Carmody et al. 2001; Goez and Zelnik 2008; Mostofsky et al. 2004; Reed et al. 2007; Reiersen et al. 2008; Seal and Bonvillian 1997; Smyth and Mason 1997; van der Smagt et al. 2007). Fifty-four studies were relevant to our purpose.
3. A third inclusion criterion was a comparison group of typically developing controls. ASD studies without a typically developing control group were not analyzed further. Nine studies did not report typically developing control groups (Ghaziuddin and Butler 1998; Green et al. 2002; Manjiviona and Prior 1995; Martos Perez and Fortea Sevilla 1993; Miyahara et al. 1997; Page and Boucher 1998; Provost et al. 2007a; Rogers et al. 1996; Wisdom et al. 2007). Forty-five studies included a typically developing control comparison group.
4. The fourth inclusion/exclusion criterion concerned data extraction problems. If studies did not report the necessary values required for coding and extracting motor coordination, motor impairment, arm movements, gait, or postural stability data, then they were excluded. Four studies were discarded based on this criterion (Coskun et al. 2009; Iacoboni and Mazziotta 2007; Martineau et al. 2004; Trevarthen and Daniel 2005).

Forty-one studies remained and they were submitted to our meta-analysis (Beversdorf et al. 2001; Coldren and Halloran 2003; David et al. 2009; Dewey et al. 2007; Dyck et al. 2006; Fournier et al. 2009; Gepner et al. 1995; Gepner and Mestre 2002; Gernsbacher et al. 2008; Gidley Larson et al. 2008; Glazebrook et al. 2006, 2008; Gowen et al. 2008; Hallett et al. 1993; Hardan et al. 2003; Hughes 1996; Jansiewicz et al. 2006; Kohen-Raz et al. 1992; Loh et al. 2007; Mari et al. 2003; Minshew et al. 2004; Molloy et al. 2003; Mostofsky et al. 2000, 2006, 2009; Muller et al. 2004; Nazarali et al. 2009; Noterdaeme et al. 2002; Ozonoff et al. 2007; Pierno et al. 2008; Provost et al. 2007b; Rinehart et al. 2006a, b, c, d; Schmitz et al. 2003; Tani et al. 2006; Turner et al. 2006; Vanvuchelen et al. 2007; Vernazza-Martin et al. 2005; Vilensky et al. 1981).

Three authors (KF, NL, & SN) independently coded the 41 studies and extracted data. Multiple group comparisons (e.g., high and low functioning autism groups) reported as separate results in nine of the 41 studies increased the number of independent meta-analytic comparisons to 51. Eight studies reported two comparisons each and one study had three comparisons. The coding system applied to each article included six categories: (a) motor coordination, motor impairment, arm movement, gait, or postural stability outcome measures and data, (b) experimental design with groups and subgroups (ASD and typically developing control), (c) sample sizes for each group, (d) intellectual ability score, (e) ASD severity scores (e.g., Childhood Autism Severity Score or Movement Assessment Battery for Children), (f) quality of research. Two authors (CH & JC) confirmed data extractions, and all authors were involved in interpreting the meta-analytic results. Characteristics of the 51 comparisons involving ASD, motor coordination, arm movements, gait, and postural stability studies are listed in Table 1.

Outcome Measures: Motor Coordination, Arm Movements, Gait, and Postural Stability

For our global questions concerning ASD and motor control impairments, seven outcome measures were identified (a) movement time/reaction time, (b) movement accuracy/error, (c) adaptation rate, (d) gait velocity, (e) center of pressure excursion, (f) balance stability, and (g) standard motor control scales (e.g., BOTMP, MABC, PDMS, PANESS, Vineland Motor Standard Score). Consistent with conventional meta-analysis techniques and in line with our research questions, we extracted data on all available outcome measures from each study. Unfortunately, deriving composite scores based on multiple outcome measures was impossible because of missing correlation values among the various outcomes (Borenstein et al. 2009). Thus, we followed standard conservative recommendations to avoid data biasing and selected only one outcome measure per study that best represented motor coordination, motor impairment, arm movement, gait, or postural control deficits. These outcome measures are listed in Table 1.

Data Synthesis and Analysis

In harmony with meta-analytic recommendations, we synthesized and analyzed our set of common ASD studies. This procedure involved (a) describing relevant characteristics of studies as well as comparison groups (see Table 1), (b) calculating standardized mean difference effect sizes for each comparison (see Table 1), (c) determining an overall effect size, and (d) identifying potential moderator variables (Borenstein et al. 2009; Rosenthal 1995; Rosenthal and DiMatteo 2001; Rosenthal et al. 2001). Once potential moderator variables were identified, additional meta-analyses were conducted to measure the contributions of subgroups to effect sizes (Hedges and Olkin 1985; Sutton et al. 2000).

Table 1 Characteristics of each ASD study used in the present meta-analysis

Study	Control		Experimental group			Primary output measures	SMD	Confidence interval (95%)	
	Total *N*	Mean age: years	Group	Total *N*	Mean age: years				
Beversdorf et al. (2001)	13	30.61 ± 12.8	ASD	10	30.8 ± 9.3	Average letter height	1.443	0.519	2.367
Coldren and Halloran (2003)[a]	7	3.78 ± 1.17	Autism	7	5.61 ± 1.08	Post shift error	1.329	0.171	2.486
Coldren and Halloran (2003)[b]	7	6.08 ± 1.49	Autism	7	5.61 ± 1.08	Post shift error	1.786	0.547	3.025
David et al. (2009)	13	11.17 ± 3.4	ASD	13	10.67 ± 3.1	Grip force at onset of load: force at 5.6 N load	0.372	−0.403	1.147
Dewey et al. (2007)	78	11.3 ± 2.4	ASD	49	10.2 ± 3.4	Gestures test BOTMP	2.215	1.766	2.665
Dyck et al. (2006)	30	8.72 ± 2.30	Autism	30	8.47 ± 2.63	Fine motor coordination	1.668	1.080	2.255
Fournier et al. (2009)	12	12.9 ± 2.1	ASD	13	11.1 ± 2.3	Center of pressure: static antero-posterior direction	1.570	0.673	2.467
Gepner et al. (1995)	12	5.6 ± 0.8	ASD	5	6 ± 1.2	Total length of center of pressure shift: eyes open	1.278	0.150	2.406
Gepner and Mestre (2002)	9	8.17 ± 2.75	Autism	3	9.42 ± 1.83	Center of pressure: total length	−0.837	−2.186	0.512
Gepner and Mestre (2002)	9	8.17 ± 2.75	AS	3	7.42 ± 2.08	Center of pressure: total length	0.630	−0.700	1.961
Gernsbacher et al. (2008)	44	8.17 ± 3.81	Autism	115	7.92 ± 3.74	Manual motor composite score	0.594	0.241	0.948
Gidley Larson et al. (2008)	10	11.7 ± 1.5	Autism	15	11.1 ± 1.6	Perpendicular displacement during reach adaptation	0.328	−0.477	1.133
Glazebrook et al. (2006)	9	25.1 ± 5.1	Autism	9	26.9 ± 6.8	Variability in displacement at peak velocity	1.009	0.028	1.990
Glazebrook et al. (2008)	18	20.6 ± 4.5	Autism	18	23.7 ± 7.9	Movement time	0.677	0.006	1.349
Gowen et al. (2008)	12	33.9 ± 13.2	ASD	12	32.0 ± 11.8	Differences in error plane deviation	1.065	0.210	1.920
Hallett et al. (1993)	5	25–36	Autism	5	25–38	Gait velocity	0.862	−0.434	2.158
Hardan et al. (2003)	41	18.6 ± 8.6	Autism	40	19.3 ± 9.9	Timed groove peg board test	0.880	0.424	1.336
Hughes (1996)	14	4.02 ± 0.18 (O)	Autism (H)	18	12.86 ± 2.56	% Pass 3/4 underhand trials	0.735	0.013	1.456
Hughes (1996)	14	3.28 ± 0.31 (Y)	Autism (L)	18	13.97 ± 3.95	% Pass 3/4 underhand trials	0.735	0.013	1.456
Jansiewicz et al. (2006)[c]	55	11.60 ± 2.72	Autism (H)	16	11.35 ± 2.47	PANESS: balance	1.509	0.899	2.118
Jansiewicz et al. (2006)[c]	55	11.60 ± 2.72	AS	15	11.35 ± 2.47	PANESS: balance	1.216	0.610	1.821
Kohen-Raz et al. (1992)	56	5–7	Autism	30	7–9	Stability index: eyes open	1.488	0.992	1.984
Kohen-Raz et al. (1992)	56	8–9	Autism	28	10–12	Stability index: eyes open	1.859	1.325	2.392
Kohen-Raz et al. (1992)	54	10–11	Autism	34	13–20	Stability index: eyes open	1.402	0.925	1.878
Loh et al. (2007)	13	1.03 ± 0.06	ASD	8	1.01 ± 0.02	Arm wave stereotypy at 18 months	0.425	−0.639	1.129
Mari et al. (2003)	20	10.44 ± 1.38	ASD	20	10.52 ± 1.51	Peak velocity in near distance task	0.377	−0.490	1.241
Minshew et al. (2004)	61	16.7 ± 10.5	Autism	79	17.0 ± 10.4	Equilibrium score: normal vision & normal support	0.418	0.080	0.755
Molloy et al. (2003)	8	10.54 ± 2.14	ASD	8	10.40 ± 2.19	Center of pressure sway: eyes open	0.881	−0.150	1.907
Mostofsky et al. (2000)	17	12.5	Autism	11	13.3	Judgment of duration	0.265	−0.500	1.026
Mostofsky et al. (2006)	24	10.68 ± 1.61	ASD	21	10.60 ± 1.98	Total errors	0.818	0.208	1.427
Mostofsky et al. (2009)	13	10.5 ± 1.4	Autism	13	10.9 ± 1.5	Total PANESS score	1.946	1.103	2.880
Muller et al. (2004)	8	28.1 ± 8.3	Autism	8	28.4 ± 8.9	Reaction time	1.157	0.098	2.216
Nazarali et al. (2009)	12	10.5 ± 1.4	Autism	12	10.5 ± 1.4	Reaction time	1.934	0.964	2.903
Noterdaeme et al. (2002)	11	8.08 ± 0.58	Autism	11	9.83 ± 2.33	Balance impairment	1.664	0.694	2.634

Table 1 continued

Study	Control		Experimental group			Primary output measures	SMD	Confidence interval (95%)	
	Total *N*	Mean age: years	Group	Total *N*	Mean age: years				
Ozonoff et al. (2007)	24	3.02 ± 0.16	Autism (NR)	26	3.15 ± 0.19	Vineland motor standard score	5.487	4.277	6.698
Ozonoff et al. (2007)	24	3.02 ± 0.16	Autism (R)	28	3.89 ± 0.16	Vineland motor standard score	5.862	4.610	7.113
Pierno et al. (2008)	12	11.26 ± 1.22	ASD	12	11.13 ± 1.22	Movement duration	1.548	0.636	2.460
Provost et al. (2007b)[d]	18	2.52 ± 0.45	ASD	19	2.53 ± 0.38	PDMS-2: locomotion	1.669	0.921	2.418
Rinehart et al. (2006a)	12	8.1	Autism (H)	12	8.1 ± 1.9	Preparation time: level 1	0.876	0.038	1.713
Rinehart et al. (2006a)	12	11.9	AS	12	12.0 ± 4.1	Preparation time: level 1	0.821	−0.013	1.654
Rinehart et al. (2006b)	21	13.83 ± 3.92	Autism (H)	17	12.42 ± 4.33	Movement time in tapping board	0.722	0.062	1.382
Rinehart et al. (2006b)	21	13.83 ± 3.92	AS	13	13.42 ± 3.67	Movement time in tapping board	0.882	0.159	1.605
Rinehart et al. (2006c)	10	10.73 ± 2.31	Autism (H)	10	10.57 ± 2.01	CV in stride length: preferred condition	1.177	0.227	2.126
Rinehart et al. (2006c)	10	10.73 ± 2.31	AS	10	10.76 ± 2.32	CV in stride length: preferred condition	0.194	−0.684	1.073
Rinehart et al. (2006d)	11	5.75 ± 1.08	Autism	11	5.83 ± 0.75	CV of velocity	0.892	0.016	1.768
Schmitz et al. (2003)	16	6.0 ± 1.0	Autism	8	7.9 ± 1.3	Latency of biceps inhibition during voluntary unloading	1.970	0.955	2.986
Tani et al. (2006)	10	N/A	AS	20	N/A	Standardized neurological rating scale	1.423	0.583	2.263
Turner et al. (2006)	8	28.6 ± 7.2	Autism	8	28.1 ± 8.3	Reaction time	0.432	−0.560	1.423
Vanvuchelen et al. (2007)	17	8.74 ± 0.97	Autism (H)	17	8.75 ± 0.92	Total MABC	1.242	0.508	1.977
Vernazza-Martin et al. (2005)	6	4–6	Autism	9	4–6	Absolute SD in sagittal plane of shoulder	1.139	0.028	2.249
Vilensky et al. (1981)	15	7.1	Autism	21	6.1	Stride phase as a % of cycle time	0.922	0.226	1.618

Studies are listed in alphabetical order

SMD standardized mean difference, *ASD* Autistic Spectrum Disorders, *AS* Asperger's Syndrome, *O* older, *Y* younger, *NR* no regression, *R* regression, *NMD* no motor delay (children without ASD who had developmental concerns without motor delay); *H* high functioning; *L* low functioning, *BOTMP* Bruininks–Oseretsky test of motor proficiency, *PANESS* physical and neurological exam for subtle signs, *PDMS* peabody developmental motor scales, *MABC* movement assessment battery for children, *CV* coefficient of variation

Special comparison groups: [a] Control group is verbal matched; [b] Control group is age matched; [c] Experimental group's mean age is combined group; [d] No motor delay served as the control group

Measuring Heterogeneity

A critical meta-analytic technique involved conducting heterogeneity tests to measure the degree of variability across studies (Hedges and Olkin 1985; Higgins and Green 2006; Rosenthal and DiMatteo 2001). Traditionally, Cochrane's Q was reported as a heterogeneity test result, however, a new test referred to as I^2 has gained popularity (Higgins and Green 2006; Rosenthal 1995). As argued by Higgins and Green, I^2 represents heterogeneity as a dispersion value with percentage units, and the technique evaluates the evidence beyond a statistical chance occurrence (Higgins and Green 2006). I^2 values for three typical heterogeneity classifications are low = 25%, moderate = 50%, and high = 75%.

Publication Bias and Fail-safe N Analysis

Publication bias arises when the probability of publishing a study increases as the effect size of its findings increases. We computed and examined three statistical techniques to determine the presence of publication bias (Hedges and Olkin 1985; Rosenthal 1995; Rothstein et al. 2005; Sutton et al. 2000). First, funnel plots graphed the effect size of individual studies against the standard error associated with each study and we used this funnel plot to determine the symmetry (Rothstein et al. 2005). Visual inspection of funnel plots evaluates symmetry across studies.

Second, Duval and Tweedie's trim and fill procedure, examines the funnel plot for quantitative representations of symmetry or asymmetry. On determining the amount of asymmetry shown in the studies, the trim and fill procedure creates a second funnel plot with imputed values inserted as close approximations to a completely unbiased distribution (Borenstein et al. 2009).

A third technique computed a classic fail-safe *N* analysis. This test determines the stability of meta-analytic results and potential bias by calculating the number of studies required to nullify an overall effect (Rosenthal 1979). The technique uses the probability value of the pooled effect size to determine the number of studies required to cancel the identified effect.

Results

Meta-Analysis on Motor Coordination, Arm Movements, Gait, and Postural Stability

Standardized Mean Difference Effect

A random effects model meta-analysis on the 51 comparisons indicated a significant overall standardized mean difference effect equal to 1.20 (SE = 0.114; $p < 0.0001$; $Z = 10.49$) with a 95% confidence interval of 0.973–1.42. This is a large, positive effect (e.g., large ≥0.80) that indicates substantial motor coordination deficits and postural stability issues in these ASD participants (Cohen 1988; Rosenthal and DiMatteo 2001). Table 1 display the individual standardized mean difference (i.e., weighted effect size) for each comparison and the values ranged from −0.837 to 5.862. Moreover, the combined motor impairments across ASD and control groups of typically developing children are readily apparent in the forest plot of individual effect sizes. As shown in Fig. 1, a majority of the individual effect sizes are to the right of the vertical line of no effect (0.00), indicating ASD motor impairments.

Further, examining the effect sizes of individual comparisons revealed two comparisons with large effects (5.487 and 5.862; (Ozonoff et al. 2007). Taking a cautious approach and removing these two outlier scores because the values were greater than 2 SD above the mean, the overall effect was still large (1.063; SE = 0.086; $p < 0.0001$).

Measuring Heterogeneity

Calculations on the current ASD and motor coordination studies revealed an $I^2 = 78.05\%$, lower limit = 71.54 and upper limit = 83.07. Such a value indicates a relatively large amount of variability in the studies (Higgins and Green 2006; Higgins et al. 2003). The high proportion of observed dispersion in the ASD studies warranted conducting a random effects model meta-analysis, as conducted. Thus, the identified summary effect (1.20) is still robust across the domain of comparisons and outcome measures in our meta-analysis (Borenstein et al. 2009; Higgins and Green 2006). Noting that caution is advised given our high heterogeneity value, moderator variable analyses were conducted to further explore the ASD and motor coordination/impairment relationships as well as reduce the amount of dispersion.

Publication Bias and Fail-Safe N Analysis

Plotting treatment effect size as a function of standard error reveals a set of ASD articles that are relatively unbiased. Visual inspection of Fig. 2 indicated a symmetrical funnel plot. Specifically, viewing the centered vertical line above the diamond indicates a relatively close match in the left and right sides of the funnel plot. Consequently, a publication bias effect was not apparent in our ASD comparisons.

The second funnel plot, Fig. 3, demonstrates an ideal symmetry of effect sizes and standard error. Usually, Duval and Tweedie's trim and fill technique imputes a value (i.e.,

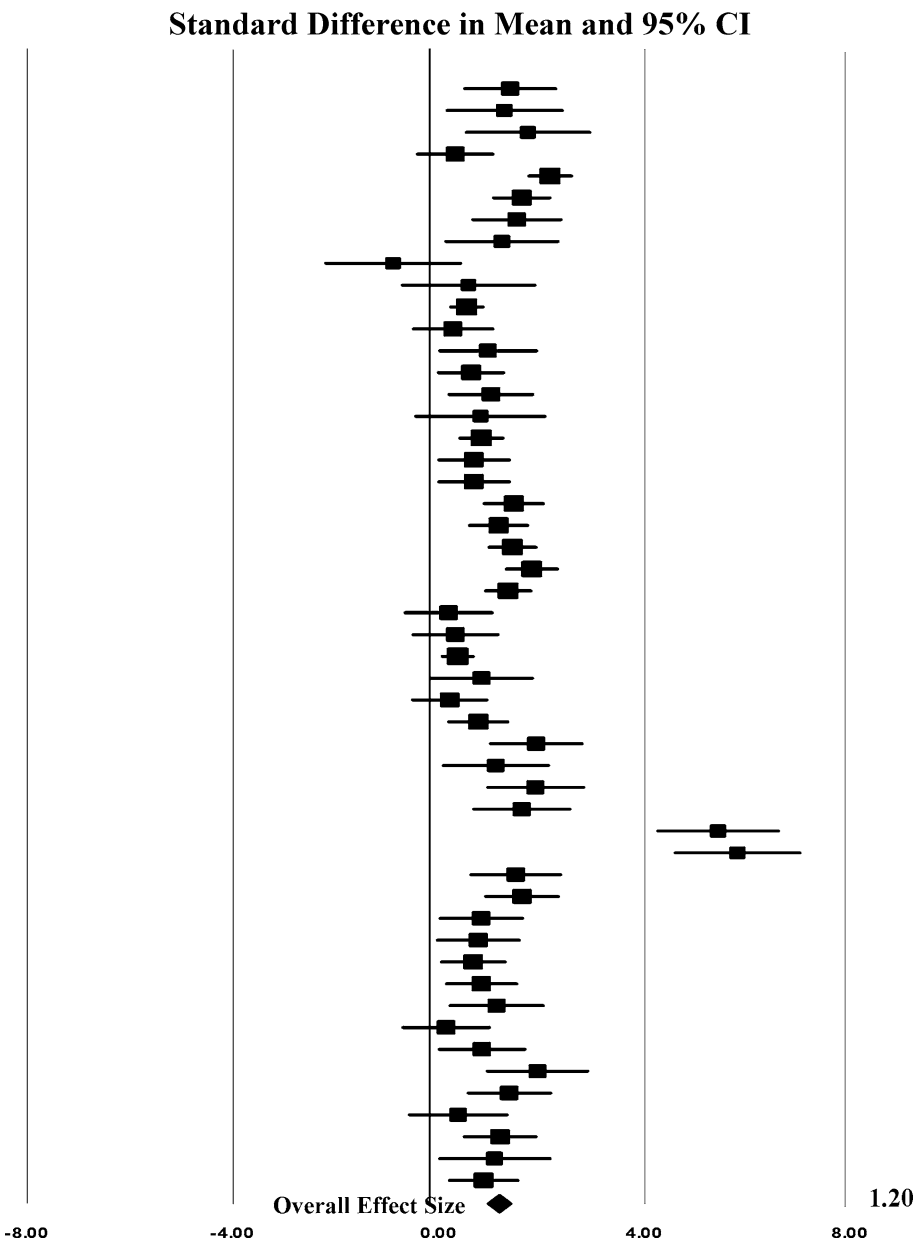

Fig. 1 Forest plot for ASD and motor coordination meta-analysis derived from a random effects model. Each line and tick mark represents an individual effect size for between-subjects comparisons. *Top* to *bottom* presentation order is consistent with Table 1. The *diamond* shape at the bottom of the forest plot is the overall effect size (1.20) for all 51 comparisons

a balanced study with a generated effect size plotted as a function of standard error) to achieve symmetry (Borenstein et al. 2009). The black diamond on the x-axis is the recalculated overall effect; practically the same value as the original large and positive effect.

As noted in the Methods, meta-analysts agree that a perfectly symmetrical funnel plot represents a best estimate of an unbiased summary effect (Borenstein et al. 2009; Rothstein et al. 2005). The overall symmetry displayed in the two current funnel plots indicates an unbiased effect. Additional information pointing to minimal publication bias comes from the fail-safe analysis in that 6,114 null effect findings were necessary to lower the cumulative effect size of 1.20 to an insignificant level. Thus, there appears to be a profound deficit in motor function in ASD compared to typically developing peers.

Moderator Variable Analysis

To investigate the identified motor coordination deficits further, we planned four moderator variable analyses. The initial moderator variable analysis examined a subgroup of studies (comparisons) that identified three types of grouping (categories) as shown in Table 1. Specifically, the three groupings involved (a) autism, (b) participants globally labeled as ASD, and (c) Asperger's syndrome versus typically developing individuals. Conducting additional mixed effects model analysis revealed a large and significant

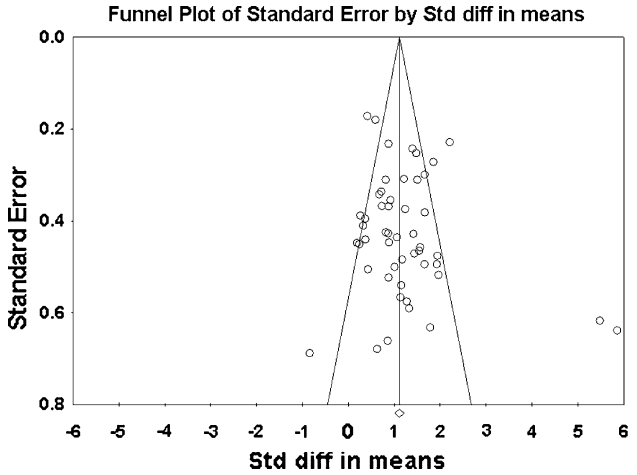

Fig. 2 Funnel plot of the comparisons for our random effects model. The x-axis is the standardized mean difference and the y-axis is the standard error associated with each comparison

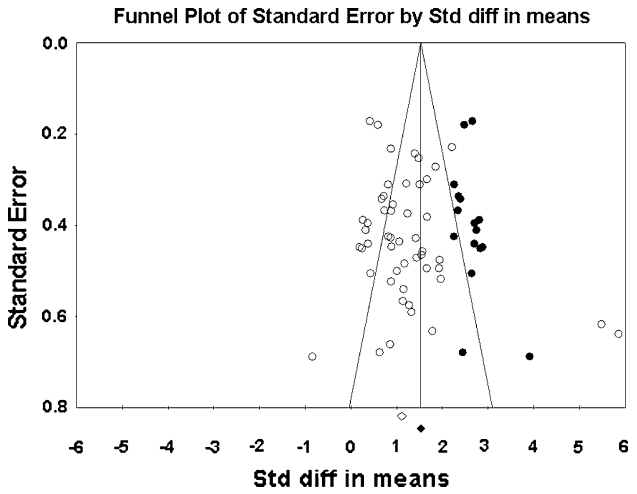

Fig. 3 Best estimate funnel plot of a symmetrical funnel unbiased effect: *open circles* and *open diamond* represent original 51 comparisons whereas *black circles* and *black diamond* represent imputed comparisons

cumulative effect of 1.13 (SE = 0.101; $p < 0.0001$; $Z = 11.21$; $I^2 = 78.05$) with lower and upper limits for the 95% confidence interval of 0.933 and 1.329. Moreover, the number of subjects in the autism group was large (696), whereas significantly fewer participants were labeled as ASD (176) or Asperger's syndrome (73). Indeed, the autism group comparisons ($n = 34$) reached significance with an effect size = 1.28 (SE = 0.15; $p < 0.0001$; $Z = 8.51$; $I^2 = 81.93$), and the 95% confidence interval was 0.985 and 1.575. Further, 10 studies/comparisons labeled participants as individuals with ASD. Meta-analysis of ASD to typically developing controls revealed a large positive effect (motor coordination deficits) 1.13 (SE = 0.228; $p < 0.001$; $Z = 4.98$; $I^2 = 72.45$), and the 95% confidence interval was 0.688 and 1.581. In contrast, even though Asperger's syndrome comparisons only involved six studies, a large summary effect was found (ES = 0.939; SE = 0.170; $p < 0.0001$; $Z = 5.535$; $I^2 = 2.80$) with a 95% confidence interval of 0.607 and 1.272. These moderator variable analyses found that each of the three categories (autism, ASD, and Asperger's syndrome) showed significantly lower motor capabilities (i.e., higher motor impairments) than control group comparisons.

A second subgroup (moderator variable) analysis compared motor coordination deficits in the upper extremities versus the lower extremities. Twenty-six comparisons investigated motor impairments in the upper extremities and 19 comparisons examined impairments in the lower extremities. The six remaining comparisons included a broad spectrum of motor assessments for both the upper and lower extremities. The overall mixed effects analysis on the full 51 comparisons indicated a large significant overall effect (ES = 0.987; SE = 0.077; $p < 0.0001$; $Z = 12.82$; $I^2 = 78.49$). Clearly, motor impairments in the extremities groupings were evident in relation to typically developing controls. Most importantly, each of the subgroup analyses revealed large reliable effect sizes: (a) upper extremities: ES = 0.88 (SE = 0.093; $p < 0.0001$ 95%; $Z = 9.49$; $I^2 = 28.49$; 95% CI = 0.701–1.006); (b) lower extremities: ES = 1.12 (SE = 0.142; $p < 0.0001$; $Z = 7.89$; $I^2 = 61.84$; 95% CI = 0.842–1.399); and (c) broad spectrum combined upper and lower extremities: ES = 2.338 (SE = 0.506; $p < 0.001$; $Z = 4.62$; $I^2 = 91.72$; 95% CI = 1.346–3.331). These subgroup findings indicated large deficits in motor coordination, arm movement, gait, and postural stability.

A third planned moderator variable analysis on age of the participants provided a valuable perspective. Initially, four distinct categories were formed: (a) infant, less than 1 year old; (b) toddler, 1–4 years old; (c) child, 5–12 years old; and (d) young adult/adult, 13 years old or older. However, across the 50 comparisons (one study was deleted because ages were not reported) many of the studies mixed the participants' ages. Thus, we combined the traditional age categories based on the individual ages reported in each study, and three separate groupings evolved: (a) toddler and child ($n = 28$ comparisons), (b) child and younger adults ($n = 9$ comparisons), and (c) younger adults and adults ($n = 13$ comparisons). Consistent with earlier findings, the mixed effects meta-analysis revealed a large positive effect that indicates motor impairments for the three combined age groups: ES = 1.065 (SE = 0.0973; $p < 0.0001$; $Z = 10.94$; $I^2 = 78.43$; 95%; CI = 0.874–1.256). Further moderator variable analysis of each age group identified large reliable effect sizes: (a) toddler and child: ES = 1.358 (SE = 0.190; $p < 0.0001$; $Z = 7.13$; $I^2 = 83.27$; 95% CI = 0.985–1.731); (b) child and younger adults: ES = 1.09 (SE = 0.240; $p < 0.0001$; $Z = 4.55$; $I^2 = 76.98$; 95%

CI = 0.621–1.562); and (c) younger adults and adults: ES = 0.924 (SE = 0.128; $p < 0.001$; $Z = 7.20$; $I^2 = 38.93$; 95%; CI = 0.673–1.176). Regardless of age groupings, participants with ASD display motor coordination, arm movement, gait, and postural stability impairments.

The fourth planned moderator variable analysis on intellectual ability of the groups indicated that 26 studies identified intellectual capabilities. However, the primary form of reporting intellectual capabilities involved a range of scores rather than group means. Further, 32 studies reported data from individuals within normal ranges for their respective ages, and 19 did not report intellectual capabilities scores. Thus, we were unable to conduct this planned subgroup analysis.

Discussion

Although gross motor impairments are frequently observed clinically in individuals with ASD, discrete studies report inconsistent findings. These inconsistencies may be attributable to the heterogeneity of behavior within the distinct diagnoses of ASD, discrepancies in the population used for comparisons, and the influence of moderating variables. Accordingly, the motor features of these disorders have received far less attention compared to communication and social interaction deficits (McLaughlin-Cheng 1998). Consequently, motor impairments may or may not be viewed as an ASD core symptom. Ben-Sasson and colleagues argue that to be treated as a core symptom, there needs to be an indication of widespread prevalence, uniqueness, and specificity to the nature of the symptom (Ben-Sasson et al. 2009).

The purpose of this systematic review and meta-analysis was to determine the degree of motor deficits within ASD across fundamental behaviors of motor performance. Our prospective and robust meta-analysis included 51 comparisons evaluating conventional outcome measures involved in motor coordination including: (a) movement preparation or planning, (b) upper extremity motor function, and (c) gait and balance. In spite of these seemingly disparate measures, the comparisons between ASD and typically developing controls revealed a significant and large effect size. This large effect clearly indicates that individuals within ASD display pronounced motor impairments when compared to neurologically normal control groups. Indeed, the precise results of the current analysis provide convincing empirical evidence to the proposition that individuals diagnosed with ASD are less coordinated and show fewer motor capabilities.

To further our understanding of the underlying motor deficits in ASD we performed several moderator analyses. First, we documented that differences in motor performance observed in our global findings are not dependent upon a specific diagnoses within ASD. Indeed, individuals diagnosed with autism, globally as ASD, or Asperger's syndrome all possessed significant motor deficits compared to the individuals with normal neurologic development. Unfortunately, we were unable to make direct comparisons within diagnoses of ASD in this meta-analysis because of the paucity of comparisons in the literature. While some studies failed to find motor performance differences between Asperger's syndrome and autism (Ghaziuddin et al. 1994; Manjiviona and Prior 1995; Miller and Ozonoff 2000), recent neuroanatomical and neurophysiologic studies suggest that there may be a neurobiological separateness (Enticott et al. 2009; McAlonan et al. 2009, 2008). For example, some reports suggest that individuals with autism exhibit a distinct gait similar to that of individuals with Parkinson's disease (Damasio and Maurer 1978; Mari et al. 2003; Vernazza-Martin et al. 2005; Vilensky et al. 1981). Recently, this potential linkage was expanded on by Hollander and colleagues (2009) who suggested a common behavioral phenomenology between autism and PD (Hollander et al. 2009a, b). Conversely, other studies of gait development and gait in children with autism suggest a locomotor pattern more similar to cerebellar ataxia (Esposito and Venuti 2008; Rinehart et al. 2006c). Taken together, these findings suggest gross motor deficits are common within ASD and that future studies are needed that directly compare individual diagnoses using structural and functional imaging as well as motor performance. These comparisons will have significant implications for the neural systems underlying ASD.

Second, significant deficits were observed in both upper and lower extremity motor performances in individuals with ASD. Though based only on the magnitude of effect sizes, motor deficiencies appear more prevalent when using gross motor evaluations that rely on postural control and mobility. An immature postural system may severely limit the emergence and performance of other motor skills. In particular, coordinated hand/head movements and the inhibition of reflexes may constrain the ability to develop mobility and hand manipulation skills; motor capabilities critical to quality of life measures (Shumway-Cook and Woollacott 2001). Further, movement disturbances such as akinesia, dyskinesia and bradykinesia may affect a person's ability to initiate, switch, continue or effectively communicate, interact socially, or perform activities of daily living (Leary and Hill 1996). Difficulties with initiation of speech (Kleinhans et al. 2005), slowness in recognizing and responding to another person (Chawarska and Shic 2009; Mirenda et al. 1983), or stopping or freezing during an activity (Vilensky et al. 1981) are observed motor phenomena that might influence social interactions and communication for individuals labeled with ASD.

Our evaluation of the moderating affects of age suggest that individuals with a diagnosis of ASD show altered motor performance compared to typically developing controls. We caution the interpretation that the modest reduction in effect size observed with increasing age provides a clue for improvement in motor function over time. The rather large discrepancies among the number of comparisons available within each age cohort likely contribute to these findings. Additionally, given the cross-sectional nature of the reported data and subsequent comparisons, we are unable to determine whether this finding is a (a) consequence of natural development, (b) product of interventional programs, or (c) combination of both.

Last, we were unable to run subgroup analyses on the influence of IQ on motor function in ASD because too few studies provided specific information regarding IQ scores or the investigators excluded individuals with intellectual impairment. We appreciate that the issue of controlling for or matching IQ in this literature is controversial. Many studies in the ASD literature considered only participants with IQ > 70, while estimates suggest that around 70% of individuals with autism have IQ's lower than that (Chakrabarti and Fombonne 2005). Further, Robinson and colleagues recently reported that executive dysfunctions such as difficulties in planning, the inhibition of prepotent responses, and self-monitoring reflect characteristic features of ASD that were independent of IQ (all participants had an IQ above 70) and verbal ability (Robinson et al. 2009). An accepted principle is that executive functions may significantly influence motor performance especially in populations with neurologic insult. However, individuals with intellectual disabilities also exhibit motor dysfunction. Thus, to provide the broadest evaluation of the spectrum of motor performance we did not exclude studies that did not control for IQ and thus, we cannot rule out the influence of intellectual disability on our identified effect sizes.

Given that our meta-analytic approach and findings confirmed that motor coordination deficits were more prevalent in individuals diagnosed with ASD than in controls with neurologically typical development is an important finding. The impairments in gait and balance, arm motor functions, and movement planning are valid. Consequently, the identified motor coordination deficit appears widespread, and thus qualifies as a core symptom of ASD (Ben-Sasson et al. 2009).

Brain Mechanisms

The observed motor disruptions in ASD may be attributed to the underlying neurobiological changes in regional and functional brain anatomy. Indeed, a wide variety of brain regions have been reported to be structurally abnormal, but because of the high heterogeneity within both ASD and the experimental designs there is often disagreement. A recent meta-analysis of structural magnetic resonance imaging studies reported consistent evidence for an increase in total brain volume as well as specific brain regions including the cerebral hemispheres, caudate nucleus, and cerebellum in autism (Enticott et al. 2009; Stanfield et al. 2008). Conversely, the corpus callosum was consistently reduced in size (Stanfield et al. 2008). Moreover, post mortem studies have detailed increased numbers of altered cortical minicolumns that may lead to a less well-organized cerebral cortex and less integration among brain regions (Bailey et al. 1998; Kemper and Bauman 1998). Indeed in vivo, Mostofsky et al. (2009) reported children with high functioning autism demonstrated diffusely decreased connectivity across the motor execution network relative to children with normal neurodevelopment. Further, Enticott and colleagues reported abnormal movement related potentials in autism and implicated the basal ganglia, thalamus, and supplementary motor area involvement as a likely source of motor dysfunction in autism.

Given that autism exists across a spectrum, conflicting findings in neuroanatomy within ASD are not surprising. McAlonan et al. (2008) found that children with high functioning autism had significantly smaller grey matter volumes in subcortical, posterior cingulate, and precuneus regions than those diagnosed with Asperger's. Compared to controls, smaller grey matter volumes in predominantly frontopallidal regions were observed in high functioning autism where as in Asperger's less grey matter was observed in bilateral caudate and left thalamus. In a separate study, McAlonan et al. (2009) found higher white matter volumes around the basal ganglia in high functioning autism than in Asperger's or controls. Both ASD groups, however, possessed greater white matter volume than controls. Conversely, both ASD groups had less frontal and corpus collasol white matter.

Taken together these mechanistic findings suggest a broad, large area with disarranged neuronal organization and cortical connectivity across ASD. Granted, motor impairments may indicate disrupted fronto-striatal pathways and basal ganglia as well as alterations in cerebellular and brain stem functions. However, the sole source or combinations of sources that cause motor coordination problems displayed in ASD await further research.

Meta-Analytic Techniques

One strength of our meta-analysis technique is the ease of determining the contribution of potential extreme score effect sizes and calculating a new effect based on the standardized mean difference technique. As seen in Fig. 1 and noted in the Results, the box shapes of individual study comparisons revealed two comparisons with large effects

(Ozonoff et al. 2007). Removing these two outlier scores (>2 *SD*) from our analysis decreases the overall effect to 1.063 (SE = 0.086; $p < 0.0001$), and I^2 is reduced considerably to 60%. Consequently, even without the extreme scores the impairments in motor coordination still produce a large, positive overall effect size.

A second meta-analytic technique identified a high degree of variability in the studies as indicated by an I^2 equal to 78%. This amount of dispersion in the 51 ASD and motor coordination comparisons warrants cautious conclusions. Such caution is consistent with recommendations by meta-analysts (Borenstein et al. 2009).

Further, the present moderator variable analyses identified three novel findings. Comparing three categories of participants, autism ($n = 696$), globally labeled ASD ($n = 176$), and Asperger's syndrome ($n = 73$) with typically developing controls demonstrated three significant and large effect sizes. These results are interpreted as additional support for our conclusion that motor impairments are ubiquitous in each type of category. Additionally, based on the magnitude of significant effect sizes, motor deficiencies are more prevalent in those diagnosed with autism. This finding is not surprising given the recent neuroanatomical and neurophysiologic studies suggesting neurobiological separateness of autism and Asperger's syndrome (Enticott et al. 2009; McAlonan et al. 2009, 2008).

Conclusions

Based on our synthesis of the existing literature and comprehensive meta-analytic techniques, we conclude that ASD is associated with significant and widespread alterations in motor performance. Indeed, motor impairments observed in individuals diagnosed with autism are greater than those impairments found in ASD or Asperger's syndrome. Recent neuroanatomical and neurophysiologic studies implicate cortical and subcortical areas including the motor cortex, supplementary motor area, basal ganglia, and cerebellar dysfunction as contributory to the observed deficits in motor planning, sensorimotor integration, and motor execution. Our current findings serve as the basis for tentatively arguing that motor deficits are a potential core feature of ASD, and that treatment of ASD should consider including interventions aimed at improving motor performances involved with motor coordination (i.e., gait and balance, arm functions, and movement planning).

Acknowledgments Kimberly A. Fournier and Chris J. Hass were supported by an award from Autism Speaks. James H. Cauraugh was partially supported by a grant from the American Heart Association. The authors of this investigation do not have any professional relationships with companies or manufacturers who may benefit from the results of the present study.

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References marked with an asterisk indicate studies included in the meta-analysis. Asterisks do not precede the in-text citations to studies

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