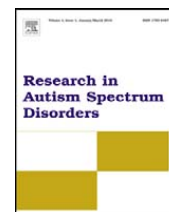




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# Research in Autism Spectrum Disorders

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## Autism severity and muscle strength: A correlation analysis

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### ABSTRACT

The current study examined the relationship between muscle strength, as measured by hand grip strength, and autism severity, as measured by the Childhood Autism Rating Scale (CARS). Thirty-seven (37) children with a diagnosis of autism spectrum disorder (ASD) were evaluated using the CARS and then tested for hand muscle strength using a hand grip dynamometer. Statistical analysis was then conducted to examine the relationship between autism severity and hand muscle strength. The model generated in the present study showed that the CARS score is a significant predictor of Max Hand Muscle Score after adjustment for age, race, gender, year of birth, and a history of prior chelation therapy. Evidence suggests that hand grip strength in children with ASD is related to the severity of the disorder. Further research is needed to determine the extent and consistency of the muscle weakness and possible treatments.

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Autism spectrum disorder (ASD) is a condition defined by its core features (American Psychiatric Association, 2000). The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text-Revised (DSM-IV-TR), published by the American Psychiatric Association for the classification of mental disorders, is used to diagnose the autistic disorder. The DSM-IV-TR criteria for autistic disorder includes: (1) qualitative impairment in social interaction, (2) qualitative impairments in communication, and (3) restricted repetitive and stereotyped patterns of behavior, interests, and activities.

Although ASD is considered a psychiatric disorder, other features, more physical or systemic in nature, are associated with autism. These features include, but are not limited to, sensory differences (Kern et al., 2006), sensory-motor deficits (Piek & Dyck, 2004), fine and gross motor problems (Provost, Heimerl, & Lopez, 2007), impairment in movement/motor skills (Green et al., 2009), balance problems (Minshew, Sung, Jones, & Furman, 2004), muscle weakness (Hardan, Kilpatrick, Keshavan, & Minshew, 2003), and hypotonia (Ming, Brimacombe, & Wagner, 2007). Studies that examined balance, coordination, movement or motor planning, and fine and gross motor skills in ASD, found problems in those areas. Although research is limited, anecdotal reports suggest that some children with autism have lower muscle strength as compared to typically

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developing children. A study by Hardan et al. (2003) examined grip strength in 40 individuals with autism without intellectual disabilities and 41 healthy controls and found that grip strength in ASD is weaker than in controls. It remains unclear how important muscle weakness is in autism and how muscle-strength may contribute to the movement, balance, and coordination problems. Furthermore, no studies have examined the relationship between muscle strength and autism severity. The current study examines the relationship between muscle strength as measured by hand grip strength and autism severity as measured by the Childhood Autism Rating Scale (CARS; Schopler, Reichler, & Renner, 1994).

## 1. Method

The study protocol received Institutional Review Board (IRB) approval from Liberty IRB, Inc. (Deland, FL). All parents signed a consent and Health Insurance Portability and Accountability Act (HIPAA) form and all received a copy.

### 1.1. Overview

Children with a diagnosis of ASD were recruited from the community to participate in the study. After explaining the study and obtaining informed consent from the parent(s), each child was evaluated using the CARS and then tested for hand muscle strength. Statistical analysis was then conducted to examine the relationship between autism severity and hand muscle strength.

### 1.2. Participants

A total of 37 participants diagnosed with an ASD were prospectively recruited from the community by using flyers and word of mouth. None of the study participants had any change in therapy or treatment (including medications) within one month prior to the study in order to limit possible confounding factors, such as problems from medication changes. None of the study participants had previously received carnitine-based therapy or previous methionine or lysine supplementation. This study was designed to exclude children who had a history of Fragile X disorder, tuberous sclerosis, phenylketonuria (PKU), Lesch–Nyhan syndrome, seizure disorder, cerebral palsy, fetal alcohol syndrome, or any history of maternal illicit drug use. Detailed information was collected on each participant regarding age, race, gender, year of birth, and a history of prior chelation therapy. Table 1 summarizes the demographic information for the subjects examined in the present study.

### 1.3. Clinical measures

#### 1.3.1. Childhood Autism Rating Scale (CARS)

Study participants were evaluated using a CARS test conducted only by a single study investigator (JKK) who observed the participants and interviewed the parent(s). Dr. Kern has been formally trained in the use of CARS and has 12 years of experience in using CARS to evaluate hundreds of children diagnosed with an ASD. The CARS was completed just prior to muscle testing.

The CARS test is a 15-item behavioral rating scale developed to identify autism as well as to quantitatively describe the severity of the disorder (Schopler et al., 1994). For CARS evaluation, a total score of about 25 is considered to be the minimum

**Table 1**

A summary of the subjects with an ASD diagnosis examined.

Descriptive information	Overall ( $n = 37$ )
<i>Sex/age</i>	
Male/female (ratio)	32/5 (6.4:1)
Mean age in years $\pm$ Std (range)	7.6 $\pm$ 3.3 (3–16)
Mean birth year $\pm$ Std (range)	2001 $\pm$ 3.3 (1992–2005)
<i>Race (n)</i>	
Caucasian	78% (29)
Minorities <sup>a</sup>	22% (8)
<i>Autistic disorder characteristics</i>	
Mean CARS score $\pm$ Std (range)	36.5 $\pm$ 5.8 (24–46.5)
Regressive ( $n$ ) <sup>b</sup>	65% (24)
Non-regressive ( $n$ )	35% (13)
Autism ( $n$ )	65% (24)
Autism spectrum disorders ( $n$ ) <sup>c</sup>	35% (13)
<i>Previous treatments</i>	
Chelation therapy ( $n$ )	11% (4)

Std, standard deviation.

<sup>a</sup> Includes participants of Hispanic, Black, Asian, or Mixed Ancestry.

<sup>b</sup> Includes participants that had a regressive event in development at any time following birth.

<sup>c</sup> Autism spectrum disorders include participants diagnosed with pervasive developmental disorder—not otherwise specified (PDD-NOS) and Asperger's disorder.

cut-off for an ASD diagnosis (Chlebowski, Green, Barton, & Fein, 2010). The CARS is a well-established measure of autism severity. The internal consistency reliability alpha coefficient is .94; the inter-rater reliability correlation coefficient is .71; and the test-retest correlation coefficient is .88. CARS scores have high criterion-related validity when compared to clinical ratings during the same diagnostic sessions, with a significant correlation of 0.84 (Schopler et al., 1994).

### 1.3.2. Hand muscle testing

After a CARS measure was completed, each participant had his/her hand muscle strength tested. The CARS was always completed before the muscle testing and not randomized in order to not influence the CARS score. The muscle strength testing was completed immediately after the CARS by a study investigator to derive their Max Hand Muscle Score using a pneumatic, adjustable squeeze pinch-gauge/dynamometer (Baseline Evaluation Instruments; White Plains, NY, USA). Participants were tested using the smallest hand grasp bulb because several of the children could only get the smallest bulb to register. Thus, the smallest ball was used for the study in order to be consistent. Each child was given as many tries as needed to register their maximum grasp reading (about four tries) measured in kilopascals (kPa) for each hand. The dynamometer has a maximum force indicator (reset) that remains at the maximum reading until reset. Multiple tries are standard for the use of this instrument. Only the maximum reading was recorded and used for analysis. Special emphasis was placed to ensure that the participant positioned the bulb in the palm of the hand and held the bulb in space to ensure that pressure was not applied by the study subject against a fixed surface. In addition, each study subject was strongly encouraged by a study investigator to give maximum effort.

This instrument is a reliable and valid method for obtaining muscle force or torque measurements in children (Berry, Giuliani, & Damiano, 2004; Hardan et al., 2003; Janssen & Le-Ngoc, 2009; Larson, Tezak, Malley, & Thornton, 2010; Merlini, Domenico, & Granata, 1995; Ties Molenaar et al., 2010) and has been used successfully in autism research (Hardan et al., 2003). In addition, the handheld dynamometer has been shown to be a valid tool for measuring overall muscle strength and for the assessment of muscle mass (Febrer, Rodriguez, Alias, & Tizzano, 2010; Leal, Mafra, Fouque, & Anjos, 2010).

### 1.4. Statistical analysis

The statistical package in SAS (version 9.1) was utilized. In all statistical analyses, a two-tailed  $P$ -value  $\leq 0.05$  was considered statistically significant. A regression analysis was done to use the CARS to predict Max Hand Muscle Score after adjusting for age, race, gender, year of birth, and chelation prior to therapy. The distribution of the raw data is shown in Fig. 1. Visual inspection of Fig. 1 shows that the relationship between the CARS and Max Hand Muscle Score does not appear to conform to a standard linear or polynomial curve (note the observation with a CARS score of 24). Therefore, instead of using a model where the relationship between CARS and Hand Muscle Score was constrained to be a straight line or quadratic or

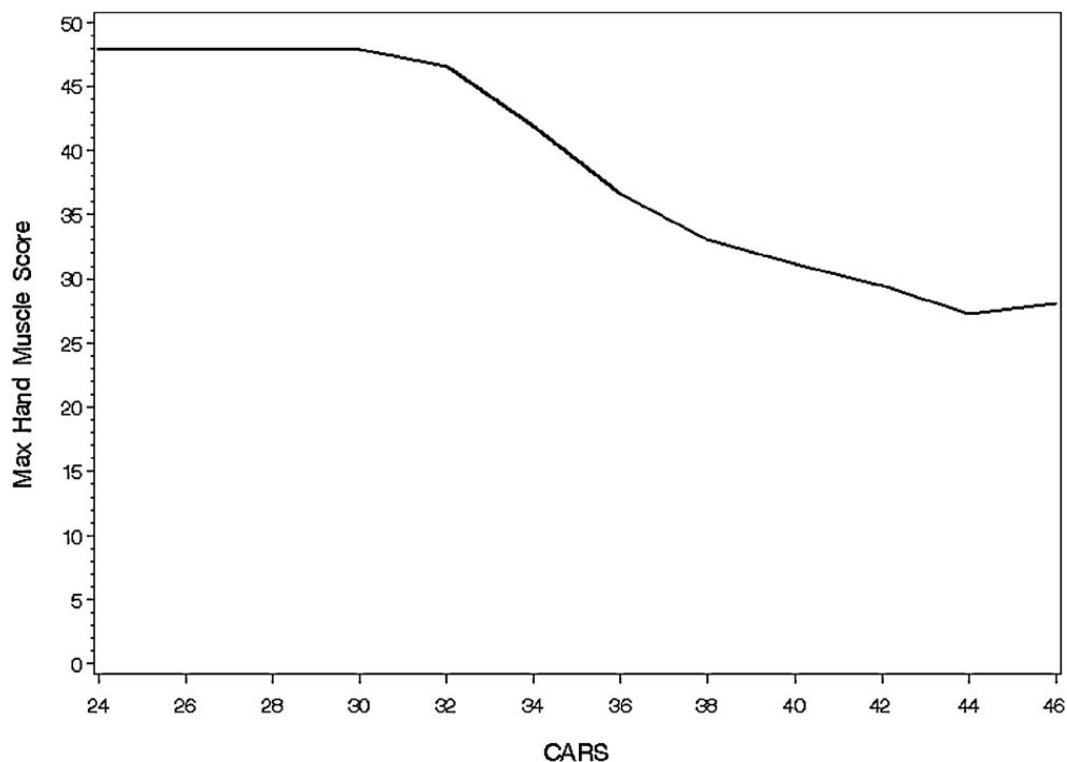


Fig. 1. A summary of the model generated in the present study showing that the CARS score is a significant predictor of Max Hand Muscle Score, as measured in kPa. The model adjusted for age, race, gender, year of birth, and a history of prior chelation therapy.

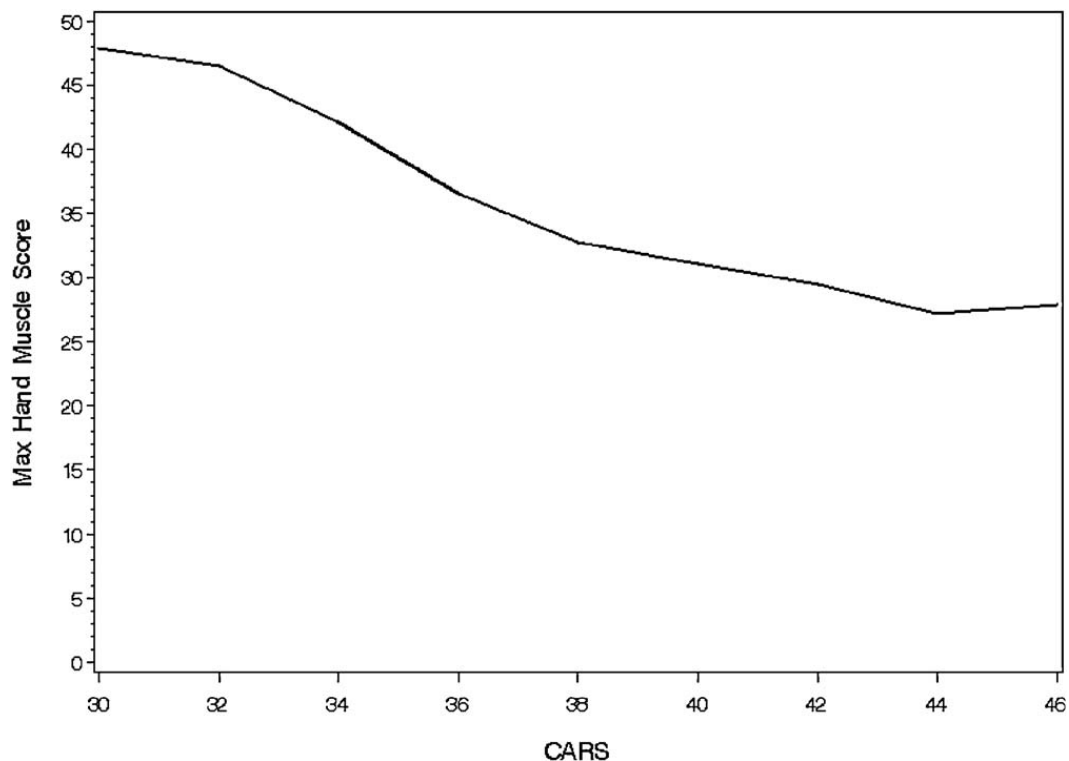


Fig. 2. A summary of the model generated in the present study showing that the CARS score is a significant predictor of Max Hand Muscle Score, as measured in kPa (excluding one study subject with a CARS score of 24). The model adjusted for age, race, gender, year of birth, and a history of prior chelation therapy.

cubic polynomial curve, a more flexible model called a spline was used in the present study (Ruppert, Wand, & Carroll, 2003). This type of model allows the data to determine the shape of the curve because the shape of the curve is allowed to change at certain locations called knots. The number of knots was chosen to give the best fit to the data.

## 2. Results

The model generated in the present study showed that the CARS score is a significant predictor of Max Hand Muscle Score ( $f = 2.6$ ,  $df = 6.24$ ,  $P = 0.0457$ ) after adjustment for age, race, gender, year of birth, and a history of prior chelation therapy. Fig. 1 shows the curve for a patient with average values for each covariate.

There is one patient with a CARS score of 24, whereas there are several CARS scores of exactly 30. To see if this value was affecting the results observed, the same model was fit without this patient. As shown in Fig. 2, excluding the study participant with the CARS score of 24 has essentially no effect on the shape of the curve between 30 and 46.

## 3. Discussion

The more severely affected a child with ASD was, the weaker the child's hand strength. The apparent relationship between autism severity and hand strength has interesting implications. First, it suggests that ASD may not be just a mental disorder, but a medical condition that may also include physical disability. Studies in ASD suggest a motor coordination component, impairments in motor development, hypotonia, and poor sensory-motor functioning in ASD (Green et al., 2009; Hardan et al., 2003; Ming et al., 2007; Minshew et al., 2004; Mostofsky et al., 2009; Piek & Dyck, 2004; Provost et al., 2007).

A second implication from the apparent relationship between autism severity and muscle strength is that treatments in autism may need to address the physical or medical disabilities. Anecdotal reports suggest carnitine, for example, may be also be beneficial. Carnitine is an amino acid and a dietary supplement that is sometimes recommended in children with ASD (Geier & Geier, 2008; Rossignol, 2009). Carnitine deficiency is commonly found associated with autistic patients (Filipek, Juranek, Nguyen, Cummings, & Gargus, 2004) and it also associated with muscle weakness (Tanner et al., 2008).

## 4. Study limitations

Measuring hand grip strength, in adults and children, has been shown to be reliable (Berry et al., 2004; Janssen & Le-Ngoc, 2009; Larson et al., 2010; Merlini et al., 1995; Ties Molenaar et al., 2010) and has been used successfully in autism research (Hardan et al., 2003). However, measuring hand grip strength in children with autism is more difficult because their level of awareness and ability to cooperate can present as confounding factors. How much the child's ability to follow directions and willingness to cooperate contributed to the variability is unknown.

## 5. Conclusion

This current study suggests that hand muscle strength in children with ASD was related to the severity of the disorder. There is a paucity of research that examines muscle weakness in ASD and possible underlying reasons. Conceivably, muscle weakness may contribute to other physical limitations, such as the movement, balance, and coordination problems. Understanding the extent of each child's muscle weakness, may provide more insight into the child's physical limitations and plan of care.

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## Conflict of interest

None.

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