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Journal
Neuropsychology, 31(7)

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Publication Date
2017-10-01

DOI
10.1037/neu0000381

Peer reviewed

HHS Public Access
Author manuscript
Neuropsychology. Author manuscript; available in PMC 2018 October 01.

Published in final edited form as:
Neuropsychology. 2017 October ; 31(7): 834–841. doi:10.1037/neu0000381.

Arithmetical Calculation and Related Neuropsychological Skills in Subjects with Isolated Oral Clefts

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Abstract

Objective—The current study examined whether the arithmetical calculation skills of children, adolescents, and young adults with isolated cleft of the lip and/or palate (iCL/P) differ significantly from unaffected control participants. Comparisons of potential neuropsychological predictors of arithmetical calculation were also conducted to determine whether these variables differ significantly for participants with iCL/P.

Methods—Participants (N = 176; 93 iCL/P and 83 Control) ranged in age from 7 to 26 years old. A standardized battery of achievement and neuropsychological skills was administered. Between group differences on math achievement was assessed through a univariate analysis of covariance. Relationships between neuropsychological measures and math achievement were analyzed separately for participants with iCL/P and Controls through hierarchical linear regressions.

Results—Arithmetical calculation was significantly lower for the iCL/P group. Rapid naming, sustained attention, and visual-spatial organization were significant predictors for the iCL/P group; rapid naming was the lone variable that was significantly more predictive of arithmetical calculation for the iCL/P group than for control participants.

Conclusions—These results suggest that inefficient verbal label retrieval related to short-term memory deficits underlie the calculation difficulties of individuals with iCL/P. These findings have implications for approaches to remediation, as well as future research.

Keywords

Oral Clefts; Arithmetic; Pediatrics; Neuropsychology; Achievement

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Oral clefts are a heterogenous group of craniofacial birth defects characterized by structural deformities within and around the mouth. Oral clefts are among the most common birth defects, occurring at a rate of 1 in every 1,250 live births (Parker et al., 2006). While some oral clefts are associated with an identifiable genetic (e.g., Alpert's syndrome) or teratogenic syndrome (e.g., Fetal Alcohol Syndrome), most occur in isolation of any distinguishable

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disorder (Jones, 1988; Jones & Jones, 2009), and as such, are described as *isolated*. Oral clefts form as a result of faulty formation, migration, and/or proliferation of the neural crest cells responsible for the development of both craniofacial tissue and central nervous system structures (Sperber & Sperber, 2009). The cleft may include the lip only (iCL), palate only (iCP), or the lip and palate (iCLP). These three subtypes are often evaluated as a group and referred to as isolated cleft of the lip and/or palate (iCL/P).

Clinical and basic research into the brain structure and neuropsychological functioning of patients with oral clefts has expanded greatly (Conrad, Nopoulos, & Richman, 2015). Neuroimaging studies have yielded evidence of structural abnormalities in the brains of both children and adults with iCL/P (e.g., Nopoulos et al., 2002; Nopoulos, Langbehn, Canady, Magnotta, & Richman, 2007; Weinberg et al., 2013). There have also been consistent findings of subtle impairments within language-related cognitive and achievement domains, including relatively lower verbal intellectual functioning (in contrast to perceptual functioning), oral expression, and reading skills (Richman, McCoy, Conrad, & Nopoulos, 2012). Research into the cognitive functioning of patients with iCL/P has demonstrated that auditory memory and rapid naming are significant neuropsychological predictors of their lower reading achievement (Collett, Stott-Miller, Kapp-Simon, Cunningham, & Speltz, 2010; Conrad, McCoy, DeVolder, Richman, & Nopoulos, 2014).

Despite a solid compendium of research into the reading outcomes of those affected by iCL/P, very little research into the mathematical skills of this population exists. This is troublesome, as mathematical development, and especially arithmetical calculation, is verbally-mediated and considerably influenced by language ability (Feifer & DeFina, 2005). Similarly, there is a high comorbidity between reading disabilities and mathematics disabilities (Butterworth, 2005). Although reading and mathematics are obviously distinct scholastic domains, they both share some essential cognitive processes. For example, both reading and mathematics rely upon successful symbol recognition and memory of symbol systems (i.e., letters or numbers; Lezak, Howieson, Bigler, & Tranel, 2012). Furthermore, accuracy and fluency in both basic reading and mathematical calculation depend on automatic verbal retrieval of over-learned facts, including recall of the phoneme-grapheme relationships required for phonetic decoding, and number-quantity correspondence necessary for counting (Feifer & DeFina, 2005; Geary, 1993).

The most consistent cognitive correlate to mathematical calculation is working memory (Swanson & Zheng, 2013). Auditory (phonological) working memory in particular has been shown to be important to mathematical achievement and predictive of calculation performance (Geary, 2013; Geary et al., 2007; McLean & Hitch, 1999). Although language has a prominent role in the acquisition of mathematics concepts, there are many other neurocognitive contributors to arithmetical calculation, including attention, visual perception, motor skills, and executive skills.

In 1980, Richman found that general language deficits in children with iCL/P were associated with poorer performance in both reading and math. Participants with general language deficits were predominately males with isolated cleft palate only (iCP). Hentges and colleagues assessed a sample of 7 year-old patients with iCL (2011) and found significant underachievement in both reading and math, with math underachievement being more severe. Finally, Wehby and colleagues have conducted a series of population studies evaluating performance of children with iCL/P on state-wide standardized assessments. Children with iCL/P were found to be lower than controls across all academic domains (Wehby et al, 2014), but this difference was not significant when compared to unaffected siblings (Collett et al, 2014).

Of the few studies that have explored the mathematics abilities in this population, those that have yielded findings suggesting that mathematics may be an area of impairment generally have neglected to elaborate what may be contributing to lower-than-expected mathematics performance. Similar to past work, the current study examined whether the arithmetical calculation skills of children, adolescents, and young adults with iCL/P differ significantly from unaffected control participants. To expand upon past work, comparisons of potential neuropsychological correlates of arithmetical calculation were also conducted to determine whether these relationships differ significantly for participants with iCL/P. Given the influence of language on both reading and mathematics and clear evidence of language impairments in individuals with iCL/P, it was hypothesized that arithmetical calculation would be significantly lower for the iCL/P group. Given that 1) reading is clearly an area of well-documented impairment for subjects with iCL/P (Conrad et al., 2015; Richman et al., 2012), 2) impaired rapid naming and working memory skills are associated with reading deficits in iCL/P (Conrad et al., 2014; Richman et al., 2012), and 3) there are overlapping cognitive processes (e.g., symbol recognition; verbally-mediated fact retrieval) required for both reading and math, it is posited that the same neuropsychological skills that are correlated to lower reading in subjects with iCL/P may also have a similar association to their math skills. Therefore, it was hypothesized that rapid naming and working memory would be the strongest correlates of arithmetical calculation for children with iCL/P in the current study.

Methods

Participants

Subjects were tested as part of a longitudinal study on cognitive and behavioral outcomes and brain development in children, adolescents, and young adults with iCL/P. Previous work from this study has reported lower verbal expression and memory in comparison to controls (Conrad, et al., 2009) as well as lower reading achievement that was strongly correlated to impairments in auditory memory (Conrad et al, 2014). The current sample comprises 100 subjects (n = 40 iCL/P and 60 Controls) who returned for follow-up assessment, as well as 76 new subjects (n = 53 iCL/P and 23 Controls) who were not enrolled in the initial evaluation. Overall, recruitment and testing of subjects for the current study took place between March 2009 and June 2012. For the 100 subjects who returned for follow-up testing, only data collected during their most recent visit were included the current analysis.

Subjects with an oral cleft were recruited from clinic lists; reports from clinical evaluations by geneticists were reviewed and only those without a potential genetic syndrome were contacted. Subjects without cleft were recruited through local advertisements. Control subjects were screened (interview with parent) and excluded for potential learning disabilities as well as exceptional academic performance (defined as participation in a talented/gifted program). This screening methodology was implemented in order to obtain a sample of subjects with average academic skills. Both case and control subjects with a history of head trauma or other major medical disorder (aside from the cleft) were excluded. The testing protocol was approved by the Institutional Review Board and all adult participants (18 years and older) and guardians of minor participants provided written consent to participant. Minor participants also provided either verbal or written assent to participate, dependent upon their developmental level. Testing was completed by a trained research assistant. Participants were monetarily compensated for their time and travel expenses.

A total of 176 participants who ranged in age from 7 – 26 years (Mean age = 17.94; SD = 4.19) were included in this study. Within the isolated cleft lip and/or palate (iCL/P) group, there were 41 females and 52 males. The unaffected control group consisted of 42 males and 41 females. Socioeconomic status (SES) was determined using a modified 5-point Hollingshead scale based on parents' self-report, with the lowest value (i.e., 1) designating the highest SES level and the highest value (i.e., 5) designating the lowest SES level. Mean SES for the ICL/P and control groups were 2.67 (SD = .61) and 2.35 (SD = .52), respectively, indicating that both fell solidly within the upper-middle socioeconomic class (i.e., from families in which adults hold college/advanced degrees; in professional or high-rank managerial positions). For 22 adult participants within the overall sample, SES data were unable to be obtained from parents, and a mean imputation was employed to account for these missing data (M = 2.51). Overall, study participants within this sample were predominantly male (52.8%), White (89.2%), and of middle or higher socioeconomic strata (84.7%). Notably, FSIQ for the iCL/P group (Standard score = 108) was significantly lower than for the control group (Standard score = 118; See Table 1). These findings are consistent with results from previous research studies indicating global intellectual ability for individuals with iCL/P that, while generally within the average range, is lower than their unaffected peers (Conrad, Nopoulos, & Richman, 2015).

It should be noted that the authors intentionally did not designate IQ as a covariate in the current study. According to Dennis et al. (2009), IQ cannot be partialed out from the effects of a congenital neurodevelopmental disorder because IQ is inextricably confounded with/by such congenital conditions. *Congenital* neurodevelopmental disorders differ from *acquired* neurological disorders in that the former involves no period of typical neurological development. The designation of IQ as a covariate is typically predicated on the hypothesis that IQ is causally linked to a correlated neurocognitive variable (e.g., memory). However, when there is an inherent difference in IQ between groups and this difference is inseparable from the independent variable to which the subject belongs, the causal mechanism cannot be determined. Even if IQ accounts for 100% of the variance in performance on a neurocognitive task, one cannot distinguish between IQ as a *cause* or IQ as an *outcome*; or a spurious association between IQ and neurocognitive measures that assess a common latent construct. (Although discussion on the statistical, logical, and methodological arguments against designating IQ as a covariate within neurodevelopmental research is well beyond the scope of the current study, readers are referred to Dennis et al.'s 2009 critical review on this topic.)

Measures

Intelligence—FSIQ was pro-rated from select subtests of the Wechsler Intelligence Scale for Children, 3rd Edition (WISC-III; Wechsler, 1991) and Wechsler Adult Intelligence Scale, 3rd Edition (WAIS-III; Wechsler, 1997a). At the start of this study, the 3rd edition was the most current version of the Wechsler scales available, and testing on this version continued throughout the length of the study. Subjects ages 7 to 16 were administered the WISC-III and those 17 and older were administered the WAIS-III. Vocabulary and Similarities were administered to calculate a pro-rated Verbal IQ (sum of scaled scores = (Vocabulary + Similarities) * 2.5), Block Design and Picture Completion subtests were administered to calculate a pro-rated Perceptual IQ (sum of scaled scores = (Block Design + Picture Completion) * 2.5). Verbal and Perceptual IQ's were combined to calculate Full Scale IQ. The Block Design subtest (standard score) was included in analyses as a measure of visual-spatial organization.

Working Memory—The Digit Span subtest (Backward Trial) from the WISC-III (Wechsler, 1991) and WAIS-III (Wechsler, 1997a) was included as a measure of auditory working memory.

Visual Memory—For visual memory, Spatial Span from the WISC-III-PI (Kaplan, Fein, Kramer, Delis, & Morris, 1999) and Wechsler Memory Scale, 3rd Edition (WMS-III; Wechsler, 1997b) was administered.

Rapid Labeling—The Color/Word Interference subtest of the Delis-Kaplan Executive Function System (DKEFS; Delis, Kaplan, & Kramer, 2001) was administered to assess rapid labeling. Time to complete trial 1 (Color Naming) was transposed so higher scores were indicative of faster (better) performance.

Sustained Attention—The Connor's Continuous Performance Test, 2nd edition (CPT-II; Conners, 2000) was administered to assess sustained attention. The score for sustained attention (number of omission errors) was transposed so higher scores were indicative of better performance.

Verbal Fluency—Subjects under the age of 13 were administered the phonemic trial of Verbal Fluency from the NEPSY (Korkman, Kirk, & Kemp, 1998) while those 13 and older were administered the Verbal Fluency subtest from the Multi-lingual Aphasia Exam (MAE; Benton, Hamsher, & Sivan, 1994). This division of tests by age was established with the original study and continued in the current methodology for consistency. Both tests evaluated the subject's ability to rapidly generate words with a specific beginning letter. To combine these tests and evaluate as one "Verbal Fluency" measure, raw scores from the MAE were used (based on three letters; CLF), and raw phonemic score from the NEPSY (based on two letters; SF) was pro-rated to be comparable to the MAE raw score.

Arithmetic—The Arithmetic subtest from the Wide Range Achievement Test, 3rd Edition (WRAT-3; Wilkinson, 1993) was administered to all subjects to evaluate arithmetic calculation.

Analyses

Because of the original design of this longitudinal study, measures were administered to some children outside the age range for normative data (i.e., DKEFS Color Word Interference for those younger than 8 years old) and raw scores had to be combined to make some tests comparable across age ranges (i.e., Verbal Fluency from the NEPSY and MAE). For these reasons, raw scores were utilized in analyses. The only exception was for WISC-III/WAIS-III Block Design; because raw scores across the different versions are not comparable on this subtest, standardized scores were used.

An analysis of covariance (ANCOVA) was conducted to evaluate the two groups' performances on the Arithmetic subtest of the WRAT-3. Participant group was the independent variable and raw score on the Arithmetic subtest was the dependent variable. Age and SES were accounted for as covariates for this analysis.

Next, to assess the neuropsychological correlates of math calculation for individuals with iCL/P and whether they differed from those of unaffected individuals with average academic achievement, hierarchical regression analyses were ran. The sample was split according to group membership (iCL/P and Control), and separate hierarchical regression analyses were then conducted for each group. The dependent variable was Arithmetic raw scores. The independent variables were entered in the following step-wise manner: Step 1) Age and SES as control variables; and Step 2) Working Memory (Digit Span Backward raw score), Visual-Spatial Memory (Spatial Span raw score), Rapid Naming (transposed DKEFS Condition 1 raw score), Sustained Attention (transposed CPT-2 Sustained Attention error raw score), Verbal Fluency (MAE/NEPSY Verbal Fluency raw score), and Visual-Spatial Organization (Block Design standard score). A simultaneous method of entry was employed for the independent variables in Step 2. Fisher's z-transformation of the partial correlation coefficients followed to determine whether there were group differences in the amount of variance explained by each neuropsychological variable.

Results

Results of the ANCOVA indicated statistically significant effects for both age, $F(1, 172) = 20.72$, $p < .001$, and SES, $F(1, 172) = 8.29$, $p = .004$, on arithmetic calculation. After controlling for the effects of age and SES, there was a significant group effect, $F(1, 172) = 15.61$, $p < .001$. Specifically, the iCL/P group's raw score on the Arithmetic subtest of the WRAT-3 ($M = 39.51$, $SD = 7.31$) was significantly lower than the control group ($M = 43.90$, $SD = 6.30$). This difference had a medium effect size ($\eta_p^2 = .08$) according to Cohen's criterion (1988). (See Figure 1 for a histogram of standard scores by each participant group.)

Results of the separate hierarchical regressions are presented in Table 2. For unaffected control participants age and SES were accounted for as control variables and were entered at Step 1, explaining 12% of the variance. The addition of the neuropsychological variables at Step 2 to the model accounted for 54.7% of the total variance for the overall model, $F(8, 71) = 10.736$, $p < .001$. The six measures within the neuropsychological block explained an additional 42.5% of the variance in Arithmetic performance for control participants after controlling for age and SES, F change $(6, 71) = 11.125$, $p < .001$. In the final model, Visual-

Spatial Memory ($\beta = .226$, $p = .021$), Working Memory ($\beta = .252$, $p = .009$), Sustained Attention ($\beta = .317$, $p = .007$), Visual-Spatial Organization ($\beta = .283$, $p = .004$) were significant neuropsychological predictors of math calculation.

For the iCL/P group, Age and SES were also accounted for as control variables and were entered at Step 1. Age and SES were shown to account for 13.3 % of the variance. After simultaneous entry of the neuropsychological variables at Step 2, the total variance explained by the model as a whole was 46.6%, $F(8, 80) = 10.604$, $p < .001$. The neuropsychological block explained an additional 38.2% of the variance in Arithmetic for the iCL/P group after controlling for age and SES, F change $(6, 80) = 10.482$, $p < .001$. Rapid Naming ($\beta = .284$, $p = .004$), Sustained Attention ($\beta = .350$, $p = .001$), and Visual-Spatial Organization ($\beta = .224$, $p = .001$) were all statistically significant neuropsychological predictors of math calculation for this group. Furthermore, there was a trend approaching statistical significance for Working Memory ($\beta = .173$, $p = .053$),

When the partial correlation coefficients of each of the neuropsychological variables were compared between the iCL/P and control groups, Rapid Naming (from DKEFS) and Visual-Spatial Memory were statistically significant (See Table 3). Rapid Naming had a stronger positive prediction value for those with iCL/P compared to controls (i.e., faster naming speed was associated with better performance on the Arithmetic subtest). Visual-Spatial Memory had a stronger positive prediction value for the controls compared to those with iCL/P (i.e., better memory was associated with better performance on the Arithmetic subtest). These findings suggesting that impaired Rapid Naming is a unique predictor of arithmetical calculation for participants with iCL/P is consistent with findings from previous research examining language functioning (Richman, McCoy, Conrad, & Nopoulos, 2012).

Discussion

The purpose of the current study was to assess differences in arithmetical calculation and related neuropsychological skills among individuals with iCL/P and unaffected children with average academic performance. Consistent with findings from Wehby et al. (2014), the current study revealed that patients with iCL/P demonstrate significantly lower arithmetical calculation performance than unaffected participants. Furthermore, the magnitude of the difference in arithmetical calculation scores between the iCL/P and control groups was both statistically *and* clinically significant, as indicated by a medium effect size (Cohen, 1988). These findings confirm the present study's major hypothesis that individuals with iCL/P perform lower in the area of arithmetical calculation when compared to unaffected peers who are functioning within the average range (i.e., excluding unaffected peers with learning disabilities or gifted/talented performance). This is a very important finding that has the potential to shift the neuropsychological cleft literature from its current focus on reading and language functioning to the broader academic achievement of this population.

Currently, there are no published research studies that have attempted to assess the neuropsychological variables involved in the mathematical skills of individuals with iCL/P. However, there have been a number of studies that have evaluated the underlying neuropsychological variables involved in the basic reading outcomes of this population, with findings consistently implicating auditory working memory and rapid naming as major predictors (Conrad et al., 2015). Given the common cognitive demands of reading and mathematics, it was hypothesized that working memory and rapid naming would be significant neuropsychological correlates of arithmetical calculation for the iCL/P group, just as they had been shown to be significant correlates of reading in previous iCL/P studies (Conrad et al., 2014; Richman & Ryan, 2003). Interestingly, the neuropsychological correlates of arithmetical calculation for the control and iCL/P groups included in this study were fairly similar. Sustained attention and visual-spatial organization were significant neuropsychological correlates of arithmetical calculation for both the control and iCL/P groups, with rapid naming being an additional correlate for the iCL/P group only and working memory and visual-spatial memory being additional correlates for the control group only. None of the other neuropsychological variables included in this study were significant correlates of arithmetical calculation for either group.

Rapid naming, a measure of automatic verbal label retrieval, was the major neuropsychological variable that distinguished participants with iCL/P from the controls. Children with iCL/P have frequently been shown to have slower rapid naming ability than their healthy peers (Conrad et al., 2009; Conrad et al., 2014; Richman & Ryan, 2003), and a study by Richman, Wilgenbusch, & Hall (2009) reported an association between inefficient verbal labeling and impaired reading skills. In light of the current study's findings regarding rapid naming, it is likely that impaired automatic verbal labeling skills underlie deficits in *both* reading and mathematics.

For the control group, visual-spatial memory was positively and uniquely correlated to arithmetical calculation performance. Within neuropsychology, visual-spatial memory is commonly thought to involve the *visual-spatial sketchpad*, a key element in Baddeley's multicomponent working memory model that holds mental representations of visual information such as shapes and colors (Baddeley, 1992). Although the visual-spatial sketchpad is logically related to performance in geometry, some research has also linked the visual-spatial sketchpad to basic mental calculation and column alignment for written arithmetic (Heathcote, 1994; McClean & Hitch,1999). In the current study, it is likely that control participants were more efficient at utilizing visual-spatial memory for arithmetical problems that could be aided by visual representations (e.g., fractions). However, the larger compendium of research has yet to consistently link visual-spatial processing to arithmetical outcomes (Fletcher, Lyon, Fuchs, & Barnes, 2007), and current understanding of the visual-spatial sketchpad's role in mathematical cognition remains limited (Feifer & DeFina, 2005).

The other distinguishing neuropsychological skill for the control group was auditory working memory. Within the general population, working memory is consistently implicated as a major cognitive correlate of basic arithmetic (Feifer & DeFina, 2005; Geary, 1993; Geary, 2013; McClean & Hitch, 1999; Swanson, 1993). The *phonological loop*, which is another crucial construct within the multicomponent working memory model (Baddeley, 1992), is frequently referenced as a framework for understanding the influence of auditory (phonological) memory on arithmetical calculation. Working memory, which is commonly assessed using number span tasks similar to those employed in the current study, has been previously associated with written arithmetical calculation (Andersson, 2008). Similarly, working memory has been shown to be a strong and unique correlate of word reading performance in children, adolescents, and young adults with iCL/P (Conrad et al., 2014). In the current study, working memory was a significant correlate of arithmetical calculation for the control group, but was just below the threshold of statistical significance for the group with iCL/P (β = .173. p = .053). These results appear to be inconsistent with previous research demonstrating a clear and significant association between performance on number span tasks and basic arithmetic (Andersson, 2008; Feifer & DeFina, 2005; Koontz & Berch, 1996; Swanson, 2013). One possibility is that insufficient statistical power prevented detection of an otherwise significant predictive relationship between working memory and arithmetical calculation for the group with iCL/P.

Lastly, sustained attention and visual-spatial organization were shown to be the strongest neuropsychological correlates of arithmetical calculation for both the iCL/P and control groups. Sustained attention is a domain-general executive skill that is critical for the acquisition of new knowledge, and disrupted or inefficient attention skills make procedural and rote recall of mathematical information challenging (Feifer & DeFina, 2005). Poor ability to marshal and sustain attention on calculation tasks makes it difficult to inhibit responding to irrelevant material, likely leading to procedural and factual errors when problem-solving. Given the vast compendium of research establishing attention as a strong predictor of scholastic achievement within both clinical (Semrud-Clikeman & Ellison, 2009) and non-clinical populations (Duncan et al., 2007), it should come as no surprise that attention was also a strong predictor of arithmetical calculation in the current study regardless of subjects' cleft status.

As noted earlier, empirical research on mathematical cognition has only demonstrated a tenuous and inconsistent link between visual-spatial processing abilities and basic calculation skills (i.e., arithmetic; Feifer & DeFina, 2005; Fletcher et al., 2007). Even so, visual-spatial processing skills are essential to a number of mathematical tasks involving quantitative analysis and spatial reasoning, including geometry, estimation, and mental problem-solving (Feifer & DeFina, 2005). Overall, however, much remains unknown about the exact influence that the visual-spatial sketchpad may have on basic arithmetical calculation, in part, because of difficulties in testing it empirically.

In contrast to previous work on mathematical skills in children with oral clefts, this study benefited from a sizable and well-defined iCL/P group for whom measures of basic arithmetic skills were available. Furthermore, participants within both the iCL/P and control groups were recruited using fairly stringent inclusion criteria to minimize potential confounds. This study's major findings corroborate recent epidemiological evidence from Wehby and colleagues (2014) indicating that iCL/P may be linked to significantly lower achievement in mathematics. Unlike the Wehby et al. (2014) study, which relied on group-administered tests of broad reading and mathematics achievement, the current study utilized an individually-administered instrument that offered more precise measurement of basic arithmetical calculation. This study was further strengthened by its inclusion of a broad range of neuropsychological measures. Consequently, the present study is the first to identify the neuropsychological predictors of arithmetical calculation in children, adolescents, and young adults with iCL/P.

Major limitations of this study include the diagnostic composition and sociodemographic characteristics of the sample. There were an insufficient number of participants within the respective iCL/P subgroups to adequately explore cleft-type differences in the neuropsychological correlates of arithmetical calculation. Furthermore, despite benefiting from a large overall sample composed of participants across a wide range of ages, there were not enough adolescent and young adult participants in either the iCL/P or control groups to permit analysis of potential age-related differences in the dependent variables. Subjects were also disproportionately White and from upper-middle socioeconomic strata. Future research studies would benefit from a sample composed of more ethnically and socioeconomically diverse subjects. Similarly, samples with greater numbers of participants diagnosed with each of the three cleft types (i.e., iCLO; iCPO; and iCLP) would help researchers clarify whether there are cleft-type differences in arithmetical calculation and its neuropsychological predictors.

As discussed earlier, IQ was not designated as a covariate in this study. We acknowledge that the difference in IQ between the iCL/P and control groups remains a *potential* explanation for the group differences observed on the other neurocognitive measures. However, the potential explanatory role of IQ cannot be ruled out through statistical adjustment by designating IQ as a covariate. An appropriate covariate, unlike IQ, is one for which there is a *causal* relationship to the outcome variable (e.g., age causing achievement, or at a minimum, serving as a proxy for educational exposure; Dennis et al., 2009). Furthermore, a covariate should not be an outcome of neither the independent nor dependent variables. Given the aforementioned confounds of congenital neurodevelopmental pathology and IQ scores (i.e., lower IQ is inextricable from the effects of the congenital neurodevelopmental disorder), age and SES were more appropriate covariates for the current study.

Emergent evidence indicating that individuals with iCL/P may be at-risk for poorer outcomes in mathematics suggests that these patients likely have more *global* academic difficulties that go beyond reading, potentially impacting all three of the core scholastic domains (i.e., reading, mathematics, and written expression). Parents, caregivers, and others involved in the long-term care of children with iCL/P should be aware of the potential risk for global scholastic difficulties. Research has long-indicated that early and targeted intervention services may help mitigate potential learning deficits that can arise in at-risk populations such as infants born with congenital defects. Due to increasingly earlier detection of oral clefts during pregnancy, any efforts to bolster perinatal and postnatal education about potential risks for learning difficulties may be beneficial to parents who otherwise may be unprepared for the cognitive sequelae of iCL/P. This knowledge may help parents take preventive measures to support their child’s pre-academic skill development and overall school readiness.

Acknowledgments

Funding/Support: This study was supported by grants from the National Institutes of Health, R01 DE014399-05 (Dr Nopoulos, PI); 5K23 DE024511-03 (Dr Conrad, PI).

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Public Significance Statement

Recognition of arithmetical concerns among children with isolated cleft and understanding of what factors are related to math skills will help in early identification and appropriate intervention.

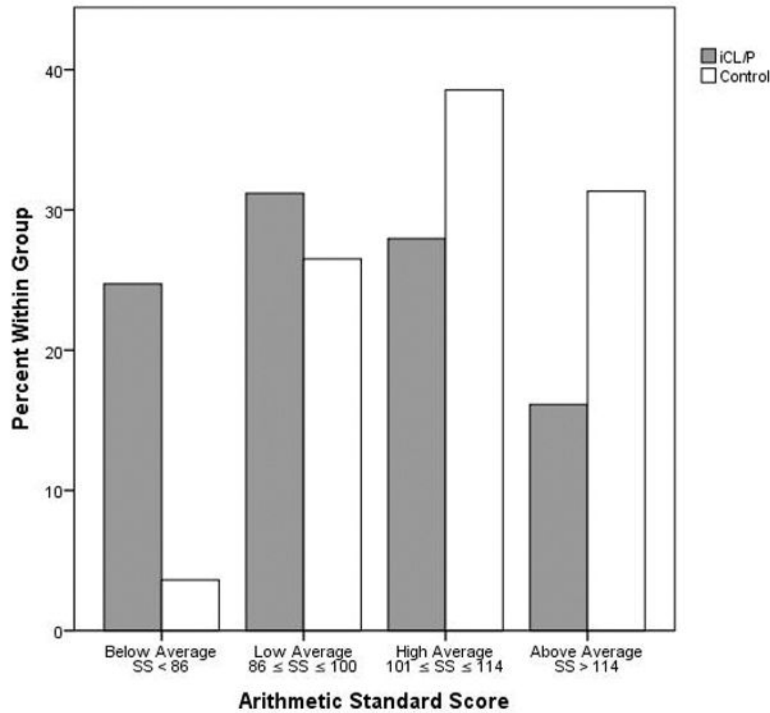

Figure 1.
Distribution of Arithmetic Standard Scores by Group.

Table 1

Descriptive and Demographic Data for iCL/P and Control Groups

Variable	iCL/P = 93			Control = 83
	iCLO (n = 22)	iCPO (n = 23)	iCLP (n = 48)	
Sex				
Male	14 (63.6%)	8 (34.8%)	30 (62.5%)	41 (49.4%)
Female	8 (36.4%)	15 (65.2%)	18 (37.5%)	42 (50.6%)
Race/ethnicity				
White	19 (86.4%)	21 (91.3%)	38 (79.2%)	79 (95.2%)
Asian American	2 (9.1%)	0	5 (10.4%)	1 (1.2 %)
Black/African American	0	1 (4.3%)	0	1 (1.2%)
Hispanic/Latino	0	1 (4.3%)	1 (2.1%)	4 (2.4%)
American Indian/Alaska Native	0	0	2 94.2%0	0
Hawaiian/Pacific Islander	0	0	0	0
Multiracial	1 (4.5%)	0	2 94.2%)	0
SES				
M (SD) =	2.36 (.50)	2.93 (.77)	2.55 (.54)	2.35 (.52)
Min =	2	2	2	1
Max =	3	4	4	4
Prorated FSIQ				
M (SD) =	108.59(15.61)	105.34 (14.62)	110.23 (13.78)	118.41 (15.99)
Min =	87	81	86	85
Max =	147	131	141	155

Note: iCL/P = isolated cleft lip and/or palate; iCLO = isolated cleft lip only; iCPO = isolated cleft palate only; iCLP = isolated cleft lip and palate; SES = Socioeconomic status.

Table 2

Hierarchical Regression of Neuropsychological Predictors of Arithmetic Scores by Group

	iCL/P					Control				
	R^2	*b*	*β SE*	*β*	*p*	R^2	*b*	*β SE*	*β*	*p*
Model 1[a]	0.133					0.122				
Age		0.421	0.153	0.277	.007**		0.509	0.195	0.281	.011*
SES		−2.885	1.250	−0.232	.023*		−2.864	1.269	−0.243	.027*
Model 2[b]	0.515					0.547				
Age		−0.206	0.152	−0.136	.178		−0.270	0.200	−0.149	.182
SES		−0.322	1.038	−0.026	.757		−0.903	1.024	−0.077	.381
Working Memory		0.684	0.348	0.173	.053		0.632	0.234	0.252	.009**
Visual-Spatial Memory		−0.104	0.380	−0.028	.785		0.722	0.306	0.228	.021*
Rapid Naming		0.189	0.063	0.284	.004*		0.002	0.128	0.001	.989
Sustained Attention		0.189	0.057	0.350	.001**		0.365	0.132	0.317	.007**
Verbal Fluency		0.014	0.056	0.022	.801		0.050	0.050	0.098	.320
Visual-Spatial Organization		0.774	0.224	0.315	.001**		0.553	0.188	0.283	.004**

Note: iCL/P = isolated cleft lip and/or palate. SES = socioeconomic status.

[a] Model 1 Predictors include Age and SES.

[b] Model 2 Predictors include Age, SES, and raw scores on measures of Working Memory; Visual Spatial Memory; Rapid Naming; Sustained Attention; and Verbal Fluency and Visual-Spatial Organization standard score.

* $p < .05$;

** $p < .01$.

Table 3

Neuropsychological Predictors by Group with Partial Correlations to Arithmetic Scores, Z- Statistics, and P-Values

	iCL/P		Control			
	n	$r_{ab.c}$	***n***	$r_{ab.c}$	***Z-statistic***	***p***
Working Memory	93	0.214	83	0.306	−0.643	0.260
Visual-Spatial Memory	93	−0.031	83	0.270	−2.004	0.023*
Rapid Naming	93	0.317	83	0.002	2.124	0.017*
Sustained Attention	93	0.347	83	0.311	0.263	0.396
Verbal Fluency	93	0.028	83	0.118	−0.589	0.277
Visual-Spatial Organization	93	0.361	83	0.329	0.236	0.407

Note: iCL/P = isolated cleft lip and/or palate.

* $p < .05$