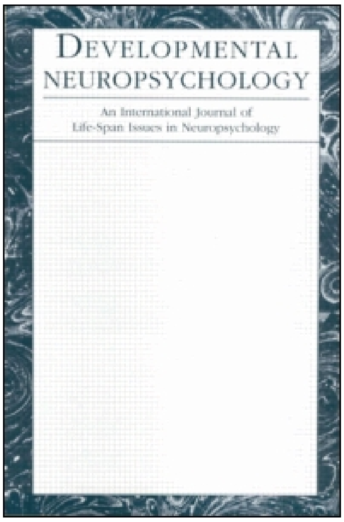

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Prevalence of Neurological Soft Signs and Their Neuropsychological Correlates in Typically Developing Chinese Children and Chinese Children With ADHD

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Prevalence of Neurological Soft Signs and Their Neuropsychological Correlates in Typically Developing Chinese Children and Chinese Children With ADHD

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This study examined prevalence of soft signs in 214 typically developing Chinese children and investigated whether soft signs are associated with attention deficit hyperactivity disorder (ADHD) in this population. Chinese children with ADHD ($N = 54$) scored significantly higher than age-matched controls on all three soft signs subscales and motor coordination correlated significantly with Stroop interference. Logistic regression supported the utility of the soft sign scales in discriminating children

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with ADHD and controls. Children with ADHD had a significant excess of soft signs, which may be a useful marker of developmental disruption in this clinical condition.

Neurological soft signs were originally defined as non-localizing neurological abnormalities that could not be related to a specific brain region or a well-defined neurological syndrome (Kennard, 1960). Along with motor impairment (Denckla & Rudel, 1978; Denckla, Rudel, Chapman & Krieger, 1985), these signs have been widely reported in both adults and children with developmental disorders (Chen et al., 1995; Heinrichs & Buchanan, 1988; Kennard, 1960). Hadders-Algra and colleagues (Hadders-Algra, 2002; Gillberg & Rasmussen, 2003) even considered these signs to reflect a global manifestation of minor neurological dysfunction.

Factor-analytic studies of neurological soft signs in adult populations suggest that these signs can be divided into subgroups. For example, Malla and colleagues (Malla, Norman, Aguilar, & Cortese, 1997) demonstrated that factors reflecting motor coordination, motor integration, sensory integration, and sequence planning were embedded in the Neurological Evaluation Scale (Buchanan & Heinrichs, 1989). In a group of 100 patients with chronic schizophrenia, Chen et al. (1995) classified neurological soft signs into motor coordination, sensory integration, and disinhibition. More recently, neuroanatomical relationships suggest that there are cerebellar, frontal, and parietal subscales; and “frontal release signs” are also considered as neurological soft signs (Chan, Huang, & Di, 2009; Egan et al., 2001).

The presence of neurological soft signs may signal potential developmental difficulties in both healthy populations (Chan & Chen, 2007; Denckla, 1974; Huisjes et al., 1980; Lunsing, Hadders-Algra, Huisjes, & Touwen, 1992) and clinical samples (Chen et al., 1995; Denckla & Rudel, 1978; Gillberg & Rasmussen, 2003; Hadders-Algra, 2002; Malla et al., 1997; Mostofsky, Newschaffer, & Denckla, 2003; Piek, Pitcher & Hay, 1999). Denckla (1974) found that typically developing children have different base-rates of motor coordination soft signs between 5 and 11 years, with a plateau for age-groups over 8 years as compared with greater differences between age-groups among the 5- to 8-year-old. Hadders-Algra and her research group (Huisjes, et al., 1980; Lunsing et al., 1992) found that children, who have shown clear signs of neurological abnormality at birth, still exhibit learning and behavioral problems after 5–11 years follow-up.

Attention deficit hyperactivity disorder (ADHD) is a developmental disorder characterized by a combination of inattentive, hyperactive, and impulsive behavior (Casey et al., 1997; Sergeant, Van der Meere, & Oosterlaan, 1999). Children with ADHD have been found to have difficulties negotiating their physical environment, exerting fine motor control (e.g., writing and tying shoe laces), and participating in social play and interpersonal relationships (e.g., in team sports and social activities) (Denckla & Rudel, 1978; Mostofsky et al., 2003; Piek et al., 1999). Impaired response inhibition, including motor overflow and mirror movements (i.e., unintentional movements that mimic intentional movement executed on the opposite side of the body), is thought to contribute to the core features of cognitive and behavioral abnormalities associated with ADHD. These cognitive and behavioral abnormalities are proposed to correspond with malfunctions of the anterior attention networks (Manly et al., 2001) including the prefrontal lobes (Barkley, 1997; Denckla & Rudel, 1978; Pennington & Ozonoff, 1996). Thus, although soft signs are not strictly localizable, they may have similar prefrontal neuroanatomical correlates as ADHD (Egan et al., 2001). Observations of atypical motor development and the “frontal release” soft signs may prove useful biomarkers for ADHD, since they appear to run in parallel with the behavioral features of the disorder.

The Cambridge Neurological Inventory (CNI) (Chan & Chen, 2007; Chen et al., 1995; Chen & Chan, 2003) is a comprehensive rating scale for assessment of neurological signs for neuropsychiatric disorders. It evaluates both hard signs (extrapyramidal signs, pyramidal signs, catatonia, and dyskinesia) and soft signs (motor coordination, sensory integration, and disinhibition). Although this scale is not as widely used as some others, such as the Neurological Evaluation Scale (NES, Buchanan & Heinrichs, 1989) in adult populations and the Physical and Neurological Exam for Subtle Signs (PANESS, Denckla, 1974) in children, impressive psychometric properties and clinical utility have been reported for the CNI in Chinese samples (Chan & Chen, 2007; Chen et al., 1995; Chen & Chan, 2003).

There is also considerable overlap between the CNI and NES with only minor differences in the subscales. Both the CNI and NES have motor coordination and sensory integration subscales. The main difference between the CNI and NES is that sequencing of complex motor acts is classified in NES and disinhibition is classified in CNI. Items pertaining to impaired sequencing of complex motor acts, such as fist, palm, and Ozeretski tests, are incorporated into the motor coordination subscale of the CNI. On the other hand, items pertaining to inhibition of motor action, such as mirror movement of the opposite hand while one hand is engaging in simple task performance, are incorporated into disinhibition subscale in the CNI. In comparing the NES and the CNI, the former is limited to motor functioning while the neurological soft sign subscales of the latter provide a wider domain of signs such as sensory integration and disinhibition in addition to motor coordination. Although many studies have examined motor control in Western samples (e.g., Denckla, 1973, 1974; Piek et al., 1999), focusing on specific aspects of coordination, gait, and balance, research examining non-Western samples with a complete range of subtle neurological signs has been limited. Moreover, preliminary findings from adult studies have suggested that there may be ethnic and cultural variations in the occurrence of neurological soft signs (e.g., Chen & Chan, 2003; Gureje, 1988). Given the promising findings of CNI from adult samples as well as its successful use in the Chinese setting, the first aim of this study was to measure a complete range of subtle neurological signs in Chinese children using this instrument. In particular we planned to sample across a wide age-range of children in order to map age-related changes in the expression of soft signs. We hypothesized that neurological soft signs would decrease with age as the neural system matures.

Diagnosis of ADHD is difficult and errors are common and, so far, there are no medical or neurological tests that can reliably diagnose this condition. The issue of diagnosis has implications for treatment and there are concerns about over-medication and the long-term effects of stimulant medication. For these reasons, finding a tool that can supplement the clinical diagnosis of ADHD or alert to a need for fuller diagnostic evaluation is a worthwhile research goal. Neurological soft signs may be helpful in this regard; therefore, a second aim was to evaluate the prevalence of soft signs in children with ADHD. Since children with ADHD are known to show impairment on motor coordination tasks and related neurological deficits (Denckla & Rudel, 1978; Mostofsky et al., 2003; Piek et al., 1999), we anticipated impairments in this clinical group on items assessing motor coordination, sensory integration, and disinhibition. More specifically, we hypothesized that, compared with healthy controls, children with ADHD would exhibit greatest impairments in functions associated with the frontal lobes.

The final aim of this study was to conduct a preliminary exploration of the clinical utility of the CNI to distinguish children with ADHD from those without the condition. We hypothesized that the neurological soft signs subscales of the CNI would be an effective instrument, in terms of sensitivity and specificity, to separate the two groups. This would mean that soft signs evaluation could potentially contribute to screening procedures to identify children in need of further diagnostic evaluation, especially for ADHD.

STUDY ONE

Method

Participants

A sample of 214 children (129 boys and 85 girls, 74.6% right handed and 5.4% ambidextrous) between the ages of 3 to 14 years was recruited from kindergartens and primary schools from medium or high socioeconomic status background in two cities in southern China (Guangzhou & Zhuhai). Children were divided into 8 groups according to their ages: 3, 4, 5, 6, 7, 8, 9, and 10-plus years old. They had no identified clinical problems based on previous annual medical screenings conducted by the schools or their school records. Participants were excluded if they had a history of head injury or neurological illness; delay of development; or sensory loss. All participants were native Chinese speaking children attending Chinese-medium mainstream schools and had normal or corrected-to-normal vision. Table 1 summarizes the demographics and IQ scores (Wechsler Intelligence Scale for Children Revised in Chinese [Gong & Cai, 1993]) of the sample. The study was approved by the Ethical Review Board of the Institute of Psychology, Chinese Academy of Sciences. Written informed consent was obtained from parents or guardians of the children.

Measures

Neurological soft signs. The soft signs subscales of the Cambridge Neurological Inventory (CNI) (Chen et al., 1995) were used to evaluate neurological soft signs. The CNI has been validated in both healthy individuals and clinical groups with schizophrenia (Chan & Chen, 2007; Chen et al., 1995; Chen & Chan, 2003). It has three subscales for soft signs: motor coordination (MC; finger tapping, repetitive finger thumb opposition, pronation and supernation, fist-edge-palm), sensory integration (SI; finger agnosia, agraphesthesia, astereognosis) and disinhibition (DI; mirror movements,

TABLE 1
Distribution of Boys and Girls by Age Group and Their IQ Scores in the Sample

Age Group	*Total*	*Number of Boys*	*Number of Girls*	*IQ (SD)*
3-year	19	9	10	97.0 (10.5)
4-year	22	11	11	101.9 (7.9)
5-year	22	11	11	102.1 (8.8)
6-year	29	16	13	105.0 (17.0)
7-year	43	29	14	106.0 (14.5)
8-year	34	21	13	108.8 (17.5)
9-year	31	21	10	108.6 (12.5)
10+-year	14	11	3	109.6 (12.5)
Total	214	129	85	104.6 (14.1)

eye blink or head movement while performing eye tracking). All items were rated by a trained research assistant. For the present study, inter-rater reliability on the soft signs subscale scores was calculated for each subscales based on the ratings of five independent cases of children. The intraclass correlation coefficients for MC, SI, and DI were 0.91, 0.82, and 0.9, respectively.

Intellectual functioning. Intellectual functioning was assessed using the Wechsler Intelligence Scale for Children Revised in Chinese (C-WISC, Gong & Cai, 1993). Five subtests, namely, Arithmetic, Vocabulary, Digit Span, Block Design and Object Assembly, were used for children over 6 years old. For children under 6, intellectual functioning was estimated using five subtests (viz., Color Match, Number-Color, Sorting, Connecting, and Numbers) from the Nonverbal Intelligence Test (Chinese version, Gong et al., 1997).

Tests of executive function. The Chinese version of the Stroop Color-Word Test (Lee & Chan, 2000) was used to assess nonspatial selective attention of the children. Due to time constraints in testing the children in school, we only administered the interference condition of the Stroop. The modified version of the Wisconsin Card Sorting Test (WCST, Nelson, 1976) was used to assess mental flexibility and categorization. The numbers of completed categories and perseverative errors were recorded. The Word Fluency Test (Spreen & Strauss, 1991) was used to assess verbal fluency. In this test, children were asked to name as many animals as they could in 1 min. The number of correctly reported animals was recorded.

Data Analysis

The prevalence and developmental pattern (reflected by the level of performance across the age groups) of the three neurological soft signs subscales and the total neurological soft signs scale (sum of the three subscales) were computed for the eight groups of participants. To assess the influence of gender and age on the neurological soft sign subscales in healthy children, a multivariate analysis of variance (MANOVA) was performed with gender and age group as IVs. Since we did not match the IQ of participants across the age groups, we controlled for the effect of this variable by including it as a covariate in other analyses. We also conducted a partial correlation analysis of performances on neurological soft signs subscales and executive functions, controlling for age and IQ in the eight groups of children.

Results

As shown in Table 2, the prevalence of individual neurological soft signs was relatively larger in the younger age groups, especially for the SI and DI subscales. The results of a MANOVA showed that there was a significant age effect on the three subscales ($F(58,588) = 7.49, p < .005$). Univariate ANOVAs showed that there was a significant effect of age on subscale scores, especially for SI, such that scores gradually decreased with increasing age (Figure 1). Boys' MC subscale score ($M = 2.56, SD = 2.21$) was higher than that of girls' ($M = 1.71, SD = 2.12$) ($F(1, 196) = 11.196, p = .001$). In addition, boys' score for the SI subscale ($M = 3.46, SD = 1.82$) was found to be higher than that of girls' ($M = 3.40, SD = 1.95$) ($F(1,196) = 4.54, p = .034$). There was no significant gender difference for the DI subscale.

MC was found to correlate significantly with Stroop interference score ($r = 0.149, p < .05$), number of WCST categories completed ($r = –0.343, p < .001$), number of WCST perseverative errors

TABLE 2
Prevalence of Individual Neurological Soft Signs in Healthy Children Among Different Age Groups

	3-year		*4-year*		*5-year*		*6-year*		*7-year*		*8-year*		*9-year*		*10+-year*	
Items	*Presence (Number of Children)*	*%*	*Presence (Number of Children)*	*%*	*Presence (Number of Children)*	*%*	*Presence (Number of Children)*	*%*	*Presence (Number of Children)*	*%*	*Presence (Number of Children)*	*%*	*Presence (Number of Children)*	*%*	*Presence (Number of Children)*	*%*
MC																
FG Thumb Tap L	1	5.3	5	22.7	1	4.5	0	0.0	3	7.0	0	0.0	0	0.0	0	0.0
FG Thumb Tap R	1	5.3	5	22.7	1	4.5	0	0.0	1	2.3	2	5.9	1	3.2	0	0.0
FG Thumb Opp L	3	15.8	8	36.4	1	4.5	6	20.7	12	27.9	9	26.5	7	22.6	3	21.4
FG Thumb Opp R	3	15.8	8	36.4	1	4.5	6	20.7	13	30.2	8	23.5	5	16.1	1	7.1
Mirror 1L	7	36.8	1	4.5	2	9.1	3	10.3	5	11.6	7	20.6	2	6.5	1	7.1
Mirror 1R	5	26.3	1	4.5	1	4.5	3	10.7	9	20.9	9	26.5	3	9.7	0	0.0
diadochokinesia L	15	78.9	9	40.9	2	9.1	1	3.4	3	7.0	7	20.6	0	0.0	1	7.1
diadochokinesia R	15	78.9	9	40.9	2	9.1	1	3.4	1	2.3	6	17.6	1	3.2	0	0.0
Mirror 2L	10	52.6	4	18.2	3	13.6	4	18.2	5	11.6	1	2.9	3	9.7	0	0.0
Mirror 2R	8	42.1	3	13.6	2	9.1	3	10.3	7	16.3	2	5.9	1	3.2	0	0.0
Fist-Edge- Palm L	6	31.6	11	50.0	9	40.9	9	40.9	18	47.9	16	47.1	8	25.8	5	35.7
Fist-Edge- Palm R	8	42.1	11	50.0	4	18.2	8	27.6	15	34.9	10	29.4	6	19.4	3	21.4
Oseretsky	4	21.1	6	27.3	1	4.5	2	6.9	3	7.0	4	11.8	6	19.4	0	0.0
SI																
Extinction	16	84.2	12	54.5	9	40.9	3	10.3	6	14.0	4	11.8	4	12.9	1	7.1
FG Agnosia L	18	94.7	19	86.4	19	86.4	23	79.3	26	60.5	16	47.1	17	54.8	9	64.3
FG Agnosia R	0	0.0	17	77.3	18	81.8	14	48.3	26	60.5	19	55.9	15	48.4	6	42.9
Stereognosia L	2	10.5	6	27.3	2	9.1	1	3.4	1	2.3	0	0.0	5	16.1	0	0.0
Stereognosia R	0	0.0	6	27.3	3	13.6	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Graphesthesia L	0	0.0	21	95.5	15	68.2	24	82.8	24	55.8	14	41.2	8	25.8	5	35.7
Graphesthesia R	0	0.0	20	90.9	19	86.4	19	65.5	21	48.8	15	44.1	12	38.7	6	42.9
L-R Orientation	17	89.5	17	77.3	12	54.5	19	65.5	21	48.8	15	44.1	9	29.0	2	14.3
DI																
saccade BLK	6	31.6	8	36.4	2	9.1	0	0.0	1	2.3	1	2.9	1	3.2	0	0.0
saccade HEAD	11	57.9	10	45.5	2	9.1	2	6.9	7	16.3	3	8.8	0	0	2	14.3
WINK	15	78.9	13	59.1	6	27.6	8	27.6	11	25.6	8	23.5	6	19.4	3	21.4
Go-no-go Stimuli	15	78.9	11	50.0	6	27.3	3	10.3	4	9.3	3	8.8	1	3.2	1	7.1

BLK: blink; DI: disinhibition; FG: finger; L: left; MC: motor coordination; R: right; SI: sensory integration.

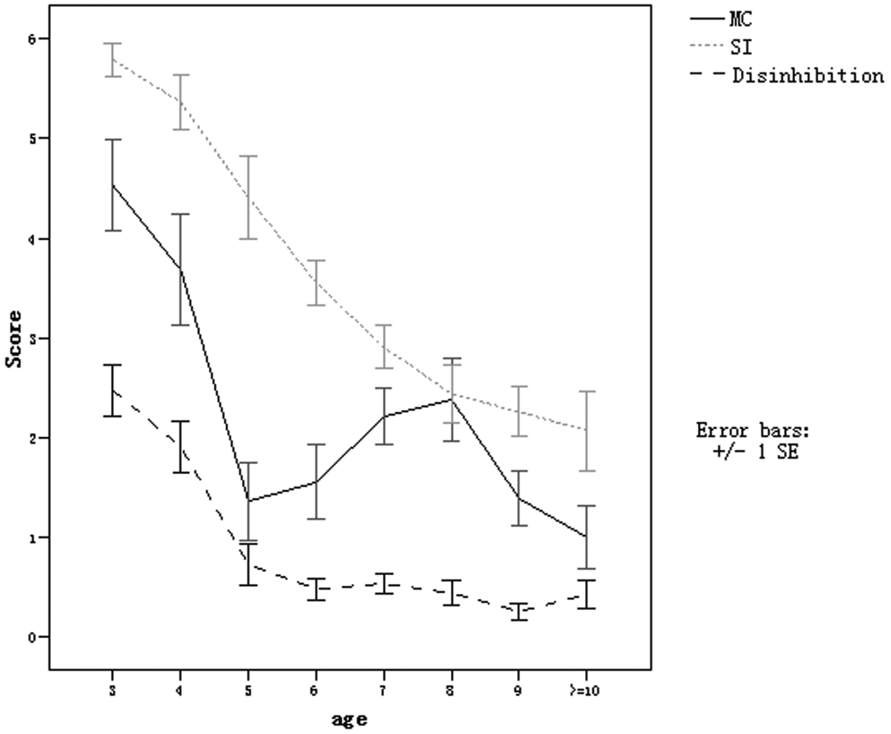

FIGURE 1 Scores on motor coordination (MC), sensory integration (SI), and disinhibition subscales among different age groups.

($r = 0.351$, $p < .001$), and verbal fluency ($r = -0.413$, $p < .01$). SI was found to correlate significantly with number of WCST categories completed ($r = -0.509$, $p < .001$), number of WCST perseverative errors ($r = 0.268$, $p < .001$), and verbal fluency ($r = -0.525$, $p < .001$). Finally, DI was found to correlate significantly with Stroop interference score ($r = -0.16$, $p < .05$), number of WCST categories completed ($r = -0.552$, $p < .001$), number of WCST perseverative errors ($r = 0.438$, $p < .001$), and verbal fluency ($r = -0.399$, $p < .001$). After partialing out IQ and age, correlation between MC and WCST perseverative errors remained significant ($r = .249$, $p = .004$) and correlations of DI with Stroop interference score($r = .235$, $p = .006$), number of WCST categories completed ($r = -.306$, $p < .0005$*), and number of WCST preservative errors (*$r = .306$, $p < .005$) also remained significant.

STUDY TWO

Method

Participants

A sample of 54 children (45 boys and 9 girls) with ADHD, was recruited through one consultant pediatrician with a clinical practice that services a large urban population in Guangdong province, China. The age range of the children was 6 to 12 years old (*M* = 8.9 years, *SD* = 1.3 years) and their average IQ was 107.9 (*SD* = 16.5), All children were native Chinese speakers and they had been diagnosed with ADHD using the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed. [DSM-IV]; American Psychiatric Association, 1994). A sample of 151 children (100 boys and 51 girls) between the ages of 6 to 13 years was selected as matched controls from the larger sample in study 1. The average age was 8.13±1.35 years and the average full scale IQ was 106.65 (*SD* = 14.86).

The study was approved by the Ethical Review Board of the Institute of Psychology, Chinese Academy of Sciences, and the relevant ethical committees of the hospitals taking part in this study. Written informed consent was obtained from parents or guardians of the children**.** Assessors of neurological soft signs were trained research assistants. They were blind to the diagnosis of the participants, that is, they were not told whether or not the children had ADHD.

Measures

ADHD participants completed the same battery of tests on neurological soft signs, intellectual functioning, and executive function as participants in Study 1.

Data Analysis

Because there were significant differences in the compositions of age and gender proportion between the ADHD and control groups, a MANCOVA with age and gender as covariates was used to compare soft signs scores between the two groups. Then, to assess the utility of the soft signs subscales of the CNI to distinguish between children with ADHD and typically developing children, we conducted two additional analyses. First, we used a binary logistic regression (LR) to identify the most parsimonious combination of CNI variables for discriminating between these two groups. Next we estimated a logistic regression model using just these terms and constructed a receiver operating characteristic (ROC) curve where cutoff points are based on each participant's predicted probability of being in the ADHD group based on the model. This provided a means of evaluating the sensitivity and specificity of the multivariate combination of neurological soft signs items. Wilcoxon nonparametric area under the ROC curve was estimated.

Finally, we conducted a partial correlation analysis, controlling for age and IQ, between performances on the neurological soft signs subscales and executive functions, in the two groups of children.

Results

MANCOVA comparisons between the ADHD and the controls showed a significant main effect of group, Wilks's lambda $F(24, 178) = 2.08$, $p < .001$. Table 3 presents the univariate group comparisons.

To identify the most salient CNI subscale predictors, we conducted a binary logistic regression to distinguish between the two groups on the basis of the hypotheses set out in the introductory section. In Step 1, MC was included as a significant predictor. In Step 2, the significant predictor was DI. Classification percentage correct improved from 75.6% in step 1 to 77.1% in step 2, which meant that the second predictor—DI contributed to the diagnosis. MC was the strongest predictor

TABLE 3
CNI Score Means and MANOVA Results for the ADHD group and Normal Comparison Groups

	Control Group		*ADHD Group*			
Items	*Score (Mean)*	*Score (SD)*	*Score (Mean)*	*Score (SD)*	*F*	*Partial* η2
MC						
FG Thumb Tap L	0.02	0.14	0.04	0.19	1.819	0.009
FG Thumb Tap R	0.03	0.16	0.02	0.14	0.037	0.000
FG Thumb Opp L	0.25	0.43	0.44	0.50	4.631*	0.023
FG Thumb Opp R	0.22	0.42	0.44	0.50	8.916**	0.042
Mirror 1L	0.12	0.33	0.33	0.48	13.322***	0.062
palphaMirror 1R	0.16	0.37	0.30	0.46	6.361*	0.031
diadochokinesia L	0.08	0.27	0.19	0.39	4.255*	0.021
diadochokinesia R	0.06	0.24	0.11	0.32	1.280	0.006
Mirror 2L	0.08	0.27	0.02	0.14	2.958	0.015
Mirror 2R	0.09	0.28	0.17	0.38	3.689	0.018
Fist-Edge-Palm L	0.37	0.49	0.85	0.36	39.040***	0.163
Fist-Edge-Palm R	0.28	0.45	0.67	0.48	25.854***	0.114
Oseretsky	0.10	0.30	0.26	0.44	7.600**	0.036
SI						
Extinction	0.12	0.33	0.24	0.43	3.244	0.016
FG Agnosia L	0.60	0.49	0.72	0.45	17.648***	0.081
FG Agnosia R	0.53	0.50	0.74	0.44	17.746***	0.081
Stereognosia L	0.05	0.21	0.04	0.19	.016	0.000
Stereognosia R	0.00	0.00	0.00			
Graphesthesia L	0.50	0.50	0.52	0.50	5.898*	0.029
Graphesthesia R	0.48	0.50	0.69	0.47	22.523***	0.101
L-R Orientation	0.44	0.50	0.44	0.50	10.373***	0.049
DI						
saccade BLK	0.02	0.14	0.09	0.29	6.629*	0.032
saccade HEAD	0.09	0.29	0.19	0.39	3.543	0.017
WINK	0.24	0.43	0.33	0.48	3.812	0.019
Go-no-go Stimuli	0.09	0.30	0.17	0.38	2.274	0.011

$*p < .05$, $**p < .01$, $***p < .001$. ADHD: attention deficit hyperactivity disorder (ADHD); BLK: blink; CNI: Cambridge Neurological Inventory; DI: disinhibition; FG: finger; L: left; MANOVA: multivariate analysis of variance; MC: motor coordination; R: right; SI: sensory integration.

of ADHD. Cases with higher MC and DI scores were more likely to be assigned to the ADHD group than to the normal comparison group.

Because two subscales were included in the final regression model, we constructed a ROC curve based on the predicted percentage of individual participant's membership. The area under the curve was .787 ($SE = .037$), $p < .0005$, indicating there was a probability of 78.7% that an individual with ADHD will have a higher score on the CNI than an individual without ADHD, the 95% confidence interval of the area under the curve ranged from 71.4 to 86.0%. When using the CNI scale to differentiate participants with ADHD from typically developing participants, the optimal cutoff predicted probability was 0.08. This cutoff resulted in a sensitivity of 92.6% (51 of 54 participants) and a specificity of 78.8% (119 of 151 participants). Thus, using this cutoff, the rate of false positive cases identified by CNI scale was 21.2%, and the rate of false negative cases identified was 7.4%.

Finally, we examined the correlations among three subscales of CNI and tests of executive function in combined samples. Correlation between MC and Stroop effect, verbal fluency were found to be significant, $r = 0.30$ ($p = .07$) and $r = 0.235$ ($p = .036$), respectively, and the correlation between SI and verbal fluency was also significant, $r = 0.233$, $p = .037$. However, none of these findings were significanct after controlling for IQ and age.

DISCUSSION

Soft Signs in Typically Developing Children

Results of Study 1 reveal substantial effects of age and gender on the CNI subscales, especially the SI subscale. Younger healthy children had a higher prevalence of neurological soft signs and there was a gradual decrement with advancing age for SI and DI as shown (see Figure 1). Boys demonstrated more MC and SI signs than girls. This study also found significant correlations between CNI subscales and some executive functions after controlling for age and IQ in typically developing children. However, no significant effect of handedness was found among the present sample.

These findings, in Chinese children, are largely consistent with those reported in Western samples (e.g., Denckla, 1974). Moreover, a strong developmental pattern was observed across the different age subgroups in this large study, with older children demonstrating lower prevalence of neurological soft signs across all the three subscales of MC, SI, and DI. The most dramatic changes in level of soft signs occurred around the 5–6-year-old age range. This parallels marked brain maturational changes around this time (Denckla, 1974). For instance, Somsen and colleagues (Somsen, van't Klooster, van der Molen, van Leeuwen, & Licht, 1997) suggested that in childhood, there are two significant and crucial neuronal growth spurts in the brain. The first one is between 6 and 7 years old; and the other one is from 9 to 11 years old. During the first growth spurt, myelination of the reticular formation and nerves linking the reticular formation to the frontal lobes occurs. This system is especially important for selective attention. These connections facilitate a child's effective use of the frontal lobes allowing the executive control of attention to mature (Shaffer, 2001). Evidence supporting this concept has been provided by Diamond and Taylor (1996) who used the tapping, a task that requires the ability to keep two rules in mind simultaneously and the ability to inhibit a strong response tendency, to show both attentional skills developed from 3–6 years. Frontal lobe gray matter increases through childhood, through the ages of 9–11 years, peaking at about age 12 years (Giedd et al., 1999).

We observed a sharp increase in prevalence of MC around 8 years old. This finding is consistent with observations that during this period there is a critical transition from an immature or childhood motor control system to a more mature adult system of motor control (Roncesvalles, Schmitz, Zedka, Assaiante, & Woollacott, 2005). Our findings are also consistent with previous studies on gender in relation to the development of neurological soft signs (e.g., Denckla, 1974). In particular, boys demonstrated higher prevalence and frequency of impairments of MC than girls. However, our observation that handedness had no significant effect on individual soft sign items is inconsistent with results reported by previous studies. The classical study showing a handedness effect on task development in healthy children (Denckla, 1974), found that significant asymmetry tended to favor the right hand in distal flexion-extension movements (e.g., hand flexion–extension, heel–toe alternation). We used different items to measure neurological soft signs and had different sample inclusion criteria. Denckla (1974) administered a more comprehensive rating scale specifically designed to capture motor disturbances. Importantly, the items included in Denckla's scale involved a complex assessment of ipsilateral and bilateral upper and lower limb coordination. Nevertheless, even when we looked at some of the individual items such as repetitive patting and pronation– supination, which are included in the MC subscale of the CNI, there was still no marked right superiority in our participants. One possible explanation of this may be that Denckla's study was limited to right-handed participants while the current study did not set such a limitation. The inclusion of both left- and right-handed participants might have diluted the potential effect of laterality on the developmental pattern of neurological soft signs.

The significant associations between neurological soft signs and executive functions suggest that these two constructs may share common neural substrates or networks (Chan & Chen, 2004; Chan, Chen, Cheung, Chen, & Cheung, 2004). Frontal cortex is critical to the development of attention and executive function in children. Executive function involves a set of complicated systems or functions that orchestrate basic or domain-specific cognitive processes (e.g., language, attention, sensory input, motor output) to achieve goal-oriented problem solving and behavior (Isquith, Crawford, Espy, & Gioia, 2005). Executive function has been found to relate to working memory, response inhibition, motor performance, interference control (Carpenter, Just, & Reichle, 2000; Livesey, Keen, Rouse, & White, 2006). Moreover, selection and orienting are completed by response inhibition, interference control, and motor performance. Brain maturation proceeds from the occipital lobes, temporal lobes, parietal lobes, and finally the frontal lobes and the first growth spurt in frontal lobes development occurs around 6–9 years old (Anderson, Northam, Hendy, & Wrennall, 2001, pp. 92–99). Thus, executive function may progressively change in this period and may parallel the integration of neurological soft signs.

Soft Signs in ADHD

In Study 2 we found that the soft signs subscales of CNI distinguished children with ADHD from typically developing controls. Specifically, MC and DI subscales differentiated the 2 groups and MC significantly correlated with Stroop effect after controlling for IQ and age.

The present result is somewhat different from the results reported by Fellick, Thomson, Sillis, Hart, and Stephanson (2001). In that study the authors examined the prevalence of soft signs in 169 mainstream pupils. They concluded that, although increased soft signs were associated with cognitive, co-ordination, and behavioral problems, they were not sensitive or specific enough for difficulties in other areas. Our studies examined soft signs in a sample of 151 typically developing Chinese children and 54 children with clinically diagnosed ADHD. In these samples, soft signs were found to be a strong indicator of ADHD. However, because we did not recruit children with other neurodevelopment disorders, our results do not tell us whether soft signs are of any more importance in ADHD than other conditions such as autism or Developmental Coordination Disorder. Thus, our results suggest that soft signs can be used as a signal to prompt more comprehensive follow-up in children, including a consideration of ADHD.

The presence of soft signs in ADHD is consistent with evidence that these children suffer a developmental delay. For example, Gustafsson and colleagues (2008) have shown that measures of general biological maturity correlate with age, but motor signs and symptoms of ADHD do not.

Thus, in ADHD neurological maturity, rather than physical maturity, appears to be a key feature of the condition. In our study MC was the strongest predictor of ADHD, and adding DI marginally improved differentiation of control and ADHD groups. In addition there was a strong correlation between soft signs and the Stroop task measurement of inhibitory performance in the ADHD group. Motor soft signs are linked to lower grey matter volumes in striatum, pallidum and thalamus (Dazzan et al., 2004.) and inhibitory function in ADHD has been found to be age-related improved in inhibitory control measured using the Change task (a task that measures inhibitory function and response re-engagement), which occur in parallel with an increase in grey matter volume in a frontal-striatal-cerebellar network in ADHD (McAlonan et al., 2009). Taken together, brain maturation, motor and inhibitory control, appear closely linked in ADHD.

The current study has several limitations. First, the relatively small sample of ADHD cases in our study and their restricted age range precluded a detailed investigation of the development of soft signs as carried out in Study 1 for the typically developing cohort. In addition, the clinical diagnosis of ADHD was not supplemented by any quantification of symptoms. Therefore we cannot say whether the extent of soft signs in ADHD is related to the severity of the condition. Information on subtypes of ADHD was not available, but this would be important to collect and examine in future studies. In Study 2, as well as investigating the prevalence of soft signs in a sample with ADHD, we also carried out a preliminary exploration of the discriminative power of CNI to separate children with ADHD from controls. This latter part would likely be better conducted in a community sample, again with assessors blind to diagnoses. In addition, because the soft signs did not show very high specificity for ADHD, at this point our results cannot be extrapolated to other groups of children suffering developmental conditions. This is an important consideration, because higher rates of soft signs are also seen in children born pre-term, children with autism and disorders involving the hypothalamo-pituitary axis (see Iannetti, Mastrangelo, & Netta, 2005). Given the current preliminary results, the differential diagnosis utility of the CNI soft signs scale should be investigated in future studies by including and comparing other clinical samples. Moreover, the samples in the current study were recruited from medium or high socioeconomic background in cities, the results obtained should be replicated in children from more varied backgrounds. Finally, since we did not use other means to evaluate soft signs in our sample of Chinese children we cannot say whether the CNI is indeed optimal for this population. Future studies are planned to compare the utility and psychometric properties of the CNI and other similar scales.

In conclusion, Study 1 provides an account of the developmental trajectory of neurological soft signs in typically developing Chinese school-aged children while Study 2 reveals that Chinese children with ADHD show high levels of soft signs consistent with delayed neurological maturation.

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