

## Clinical Research

# Neurocognitive Attention and Behavior Outcome of School-Age Children with a History of Febrile Convulsions: A Population Study

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**Summary:** *Purpose:* A prospective population-based case-control study was performed to ascertain whether febrile convulsion (FC) in early childhood is associated with neurocognitive attention deficits in school age.

*Methods:* A total of 103 children, confirmed to have FC by age 3 years from a population survey of 4,340 live-birth newborns in Tainan City, Taiwan, was followed up until at least age 6 years. An achievement test, behavioral ratings, and computerized neurocognitive battery assessing various subcomponents of attention were given to 87 FC children (FC group) and 87 randomly selected population-matched control (CC group).

*Results:* Compared with the CC group, the FC group did not have scholastic performance or behavioral outcome disadvantage. Overall FC group performance was distinguished by sig-

nificantly higher scores in the achievement test and fewer missing errors ( $p < 0.005$ ) and commission errors ( $p < 0.05$ ), less variability in reaction time ( $p < 0.005$ ), and a nonsignificant trend of impulsivity. Attention performance of the FC and CC groups were comparable. Within the FC group, age at onset, complex FC, recurrence of FC, development of unprovoked seizures, or prior use of phenobarbital had no adverse effects on neurocognitive attention outcome.

*Conclusions:* This population study suggests that FC in early childhood does not have adverse effects on behavior, scholastic performance, and neurocognitive attention. On the contrary, the FC group demonstrated significantly better control of distractibility and attention at school age. **Key Words:** Febrile convulsion—Attention—Neurocognition—Outcome.

Febrile convulsion (FC) is the most common seizure disorder in children, affecting 2–4% of children before age 5 years (1,2). Although the natural history of FC is well understood, the cognitive and behavior outcomes have long been a subject of controversy (3,4). Such controversy is the result of differences in case selection, neuropsychological measures, and the duration of follow-up (1–5). Most hospital-based studies have found relatively high rates of mental retardation (8–22%), behavioral disturbance (30%), and academic difficulties at follow-up among children with FC (6–9). In contrast, population-based studies have demonstrated comparable intelligence and academic performance in FC children and controls (10–15). Although there was more psycho-

logical disturbance and anxiety rated by the mothers of FC children, there was no significant evidence of FC effects on behavior in the population-based studies (10,14).

The association of mesial temporal sclerosis with FC, as demonstrated by neuropathologic and neuroimaging studies, raised the possibility of subtle sequelae of late emergence (16–18). Although there is a long interval between initial FC and later onset of complex partial seizures, there may be subtle neurocognitive dysfunction, at least at high cortical levels, in these vulnerable cases during the formative school years. Most neurocognitive outcome studies on FC have emphasized global measures of scholastic achievement, intelligence tests, and behavior questionnaires (6,7,10–15). Computerized neuropsychological testing, however, may help detect non-clinically evident neurocognitive dysfunction in an objective and sensitive way (19,20). Attention appears to involve a complex set of abilities that involves motor and

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social development and multiple cognitive processes (21). The performance on simple focus attention tasks indicates vigilance, whereas difficult tasks with several attentional requirements (i.e., information processing, inhibition of response, planning, attention shift, sustained attention, and choice reaction) are sensitive measures of neurocognitive components (22). Attentional difficulties also have been found to be closely associated with educational problems in children with seizure disorders (23). Only one study showed disrupted sustained attention on continuous performance tests in 15 FC children. It was, however, a hospital-based study with a small sample (24). The literature currently contains no study that directly evaluates on a population basis neurocognitive attention in school-age children with a history of FC.

Thus our group conducted a population study of provoked seizures, including FC, in Southern Taiwan (5,25, 26). To ascertain whether FC in early childhood may be associated with behavioral problems and specific neurocognitive function deficits, the academic performance, behavioral ratings, and different subcomponents of neurocognitive attention, of school-age children with and without a history of FC were assessed and compared. Furthermore, to identify the risk factors associated with the neurocognitive disadvantages among FC children, the FC characteristics and the major biological, environmental, and genetic variables were compared between FC children with and without neurocognitive attention deficits.

## SUBJECTS AND METHODS

### Eligibility

A two-phase study design was used to identify patients with FC, as described previously (5,25,26). The first phase screened the entire study population with telephone survey, whereas the second phase evaluated the possible FC subjects with a standard home interview. FC was defined according to the U.S. NIH Consensus Development Conference criteria (27). Children with evidence of intracranial infection or with previous afebrile seizures were excluded. Simple FC was considered to be a single, generalized seizure lasting <15 min, and complex FC as a partial seizure, a seizure lasting >15 min, or repeated seizures within 24 h of illness (5,26).

### Febrile convulsion group (FC group)

All the live-birth certificates of children born between October 1989 and June 1990 in Tainan City, Taiwan (total population, 709,440) were retrieved from the Department of Health Administration. A total of 4,860 children were born in the study period. After excluding 243 families without a phone, 4,617 (95%) families were included in the telephone survey. A telephone interview for seizure history was attempted for each family when the child reached age 3 years. Parents or main caretakers

were asked, "Has the child ever had any form of convulsion or episode of consciousness disturbance?" For children with suspected seizures, parents were further asked, "What were the clinical manifestations at the first seizure? Did the seizure occur during fever? At which hospital or clinic did you seek help? What was the diagnosis?" (25,26). After the exclusion of 277 families whose whereabouts were unknown ( $n = 47$ ) or who had moved out of the city ( $n = 176$ ) or refused to participate ( $n = 54$ ), 4,340 (94%) families were actually interviewed.

All patients identified by telephone survey as possibly having FC were investigated further with a home interview. A research assistant called and obtained consent from the parents for the home visit. At each home visit, the parents were interviewed with a standard questionnaire. The research assistants first asked to speak to the person who witnessed the reported seizure. They then asked a series of questions to verify the event as a seizure. Descriptions of the events were compiled from this part of the interview, and from the descriptions, the occurrence of seizure was determined and then classified as simple or complex (25,26).

The questionnaire included sociodemographic information, pre- and perinatal history, developmental history, a description of the reported first FC, and family history of seizure disorders. The interrater reliability of the home visit questionnaire among the research assistants was 0.95 (26). The medical records of the child at the time of FC also were retrieved from the clinicians and hospitals, as possible. After the home interview, each questionnaire was reviewed and verified by two pediatric neurologists (C.-C. Huang and Y.-C. Chang). Inquiry regarding family history of FC was made among not only the affected relatives but also the nonaffected ones after home visit by telephone interview of the family member.

### Prospective follow-up

All the identified FC children were followed up yearly for any recurrence of FC and subsequent unprovoked seizures until they were at least age 6 years. Recurrent FC was verified from medical records in hospitals and from practicing pediatricians. Medical records were obtained for all children seen in hospitals and 93% from practicing pediatricians.

### Population control group (CC group)

The CC group came from a nationwide sample among school-age children attending regular classes (28). The nationwide sample was selected according to the characteristics of urbanization level in Taiwan districts by probabilities proportional to size method. A total of 56 elementary schools were sampled randomly from 216 schools in Taiwan. The nationwide sample had 213 children aged 6–8 years, and a questionnaire was completed by the parents of these children regarding any seizure history of the child. The questionnaire also included data

regarding the family's socioeconomic status. The CC group consisted of 87 children from this nationwide sample age-matched to the children in the FC group (within 4 months of birth) by individual. Each of the age-matched controls was selected by using a random-number table from the age-matched nationwide sample to each child in the FC group. An exclusion criterion of history of any seizure was imposed in the selection of the controls.

### Achievement and behavioral survey

Both FC and CC groups took the Chinese Achievement Test. It is a standardized test in Taiwan, and the normative data have been collected from a total of 7,166 students from first to seventh grades in the school district of Taiwan. The mean  $\pm$  SD of normal standard score was  $50 \pm 10$  (29). In addition, teachers were asked to rate the children's class performance as regards language skills, arithmetic skills, and general knowledge. Those below the 10th percentile were defined as abnormal. Parents and teachers also completed Conners' Parental and Teacher Rating Scales, respectively, for behavior problem (30).

### Neuropsychological examination for attention

#### Method

The neuropsychological testing was performed on the FC and CC groups in a small private room at their own schools. The tasks were all computerized and administered in real time. The stimuli were generated by a large plastic box with a gray front panel  $\sim 30$  by 34 cm. Round holes were cut into the panel. Each hole was fitted with either a red or green light-emitting diode (LED). The holes were arranged in pairs, one red and one green LED to a pair. The pairs were arranged in an array of five rows and nine columns. Children were provided with two hand-held switches, each held in the hand like a joystick, one switch for each hand, each with a top button operated by the thumb. Children reacted to the stimuli by pushing the appropriate button(s) as instructed before the task. Each task required a brief explanation, but basically was self-taught in a brief practice session. The child was instructed to respond as rapidly as possible. The entire test took  $\sim 20$ –30 min, depending on the child's speed and accuracy (28).

Each child took part in a brief practice session for each task before examination. Each task consisted of a series of trials involving the child reacting in a specified manner to a specified illumination pattern. Each trial was preceded by a warning tone, which was followed, at a random interval ranging from 1.0 to 4.4 s, by the switching on and displaying for 1.5 s of a light or pair of lights. The screen then remained blank for 1 s. During this period of 2.5 s (1.5 s of illumination, and 1 s of blank time), the subject could respond. For purposes of scoring,

tone-to-illumination waits of 1–2.4 s were defined as short intervals, and 3.0–4.4 s as long intervals.

The test included five tasks of increasing complexity. For all tasks, the child was instructed to push the button as soon as possible after stimulus, and the response speed was recorded (hand motor speed). The five tasks were

1. Simple reaction task: Only the central LED pair in the array was used for this task. The child was given the left-hand switch and was instructed to push the button when the red LED came on. The light always followed the tone, but at a variable interval. There were 18 trials in this half of the task. The task was repeated for the right hand, this time with a green LED.
2. Searching task: The task was identical to the first, except that the LED could appear at any portion of the array.
3. Go-no-go task: This task involved only the left hand. A warning tone preceded the visual stimulus by the same variable interval. The child was instructed to push the button on seeing a red LED, but not to push the button if the green LED of the pair was simultaneously illuminated. The LED pair could be located anywhere in the array. There were 36 trials to the tasks.
4. Go-no-go task with distracters: An overlay was mounted on the panel, thereby putting an image immediately above 36 of the LED pairs (four of the rows). The image was either of a pair of alternate but similar images. One image of the pair was mounted alone at the top of the panel. Only the right hand was tested. After the warning tone and variable waiting period, a green LED below one of the images was illuminated, indicating that image. The child was instructed to push the button only when the image designated by the LED was identical to the image mounted at the top of the panel. The task involved 36 trials.
5. Principle reverse task: This task is the inverse of task three, in that the child was instructed to press the button when both members of an LED pair were illuminated, and not for the illumination of a single LED. Again, only the left hand was tested, again for 36 trials.

#### Recording

Responses occurring after the tone but before the illumination or responses before 100 ms were considered *impulse errors*. Responses delayed  $>2.5$  s after illumination were recorded as *missing errors*. *Commission errors* resulted from a failure to inhibit the response to the no-go stimulus. If there were more than eight errors in that task, it was defined as *failed*. *Short-duration sustained attention* was defined as the difference of total errors between the short interval after the tone (1–2.4 s) and the

long interval after the tone (3.0–4.4 s) in simple reaction task. *Relatively long-duration sustained attention* was defined as the difference of total errors between anterior half part and posterior half part of simple reaction task. The *mean reaction time* (MRT) and *variability of speed* were defined as the mean and standard deviation of the reaction time of the correct reaction if the correct trials were greater than three fourths of the total trials in that task.

The attention mechanism was further divided into four major components according to Cohen's classification (31): (a) *Sensory selective attention*, including simple reaction (total errors in simple reaction task), searching skills (the difference of total errors between searching task and simple reaction task), and filtering skills (the difference of total errors between go–no-go with distracters task and go–no-go task); (b) *Response control*, including impulsivity (impulse errors in simple reaction task), and inhibitory control (total impulse and commission errors in go–no-go with distracters task and go–no-go task); (c) *Attention capacity*, total errors in principle reverse task; and (d) *Sustained performance*, including short duration and relatively long duration sustained attention. Those who had errors greater than the 10th percentile of the control group or who failed that task were defined as abnormal.

#### **Risk factors for attention deficits within FC group**

The FC children with attention deficits were categorized as deficits in sensory selective attention, response control, attention capacity, or sustained performance. Four major risk factors for attention problems were assessed among the FC group (26). The biologic risk factors included prior neurodevelopmental problems, pre- and perinatal events (intrauterine smoke exposure or alcohol intake, maternal hypertension or diabetes during pregnancy, small-for-gestational age, or hospitalization in the neonatal intensive care unit). The environmental risk factors included low socioeconomic status. The genetic risk factors included family history of seizures. The seizure risk factors included FC onset before age 1 year, complex FC, recurrent FC, subsequent unprovoked seizures, and prior use of antiepileptic drug (AED) therapy. To identify the risk factors for neurocognitive attention deficits among FC children, the major risk factors were compared between FC children with and without attention problems.

#### **Statistics**

Data comparison between groups for continuous data was made with the Wilcoxon rank sum test, and for categorical data with Fisher's exact test. The univariate and multivariate analysis of risk factors for four neurocognitive deficits among FC children were performed by using the LogXact and StatXact (CYTEL Software Corporation, Cambridge, MA, U.S.A.). All statistical tests

were two-tailed, and a *p* value <0.05 was considered statistically significant.

### **RESULTS**

A total of 4,340 parents of 3-year-old children in Tainan City, Taiwan, were contacted by telephone for any history of seizure. Among them, 122 children were reported to have had FC. After case validation and excluding 19 cases of central nervous system infection, breath-holding spells, and other nonconvulsion events, 103 children had an event that met the criteria for FC. The mean FC onset age was 21.3 months, and 17 children had complex FC. Prospective follow-up was undertaken on these 103 FC children when they were at age 6 years or older. By age 6 years, 31 (35.6%) of them had recurrent FC, and subsequent unprovoked seizures developed in four (4.6%). Three of the children had taken phenobarbital (PB) for FC prophylaxis for a mean duration of 3.6 months. Excluding 16 children whose parents did not give consents for the tests, 87 FC children completed the examinations, which included achievement test, scholastic performance, behavioral ratings, and neurocognitive examination for attention. These 87 FC children all attended regular classes in elementary school. None of them had epilepsy or were taking AEDs at the time of neuropsychological examination.

At the time of neurocognitive examination, the age of the FC group was comparable with that of the CC group (mean  $\pm$  SD,  $84.6 \pm 4.3$  vs.  $85.8 \pm 3.6$  months). The gender distribution also was comparable (35 girls, 52 boys in FC group, and 38 girls, 49 boys in CC group). There was no significant difference in the parents' socioeconomic status between the two groups.

#### **Comparison of achievement test and behavioral ratings between FC and CC groups**

The FC group had significantly higher scores on the Chinese achievement test than the CC group (*p* < 0.05). Nine children in both groups had scholastic difficulties (less than 10th percentile of the school class) in reading, arithmetic, or knowledge, according to the teachers' rating. The proportion of children in the FC group who had reading difficulty (1:9) was not significantly different from that of CC group (6:9). The same result was obtained for the arithmetic problem (3:9 vs. 5:9), and for the knowledge problem (7:9 vs. 8:9). By the Conners' Parental rating scale, the proportion of children with conduct problem, impulsivity–hyperactivity, anxiety or high hyperactivity index was 10.3% (9:87) in FC group and 18.4% (16:87) in CC group. Although the FC children had less frequency at every aspect of these behavior problems, no significant difference was found by the Fisher's exact test. By the Conners' Teachers' rating scales, the proportion of conduct problems, inattention–passivity, hyperactivity or high hyperactivity index was

**TABLE 1.** Differences in the achievement and behavioral outcome between febrile convulsion and control group

Parameters	FC group (n = 87)	CC group (n = 87)
Chinese achievement test <sup>a</sup>	53.5 ± 1.7	48.5 ± 1.1 <sup>d</sup>
Scholastic difficulties (no.) <sup>b</sup>	9	9
Reading problems	1	6
Arithmetic problems	3	5
Knowledge	7	8
Behavior problem by Conners' parental rating scale (no.) <sup>c</sup>		16
Conduct problems	9	8
Impulsivity-hyperactivity	5	0
Anxiety	1	6
Hyperactivity index	2	10
Behavior problem by Conners' teacher rating scale (no.) <sup>c</sup>		8
Conduct problems	11	4
Inattention-passivity	6	4
Hyperactivity	2	0
Hyperactivity index	4	0

FC, febrile convulsion children; CC, control children.

<sup>a</sup> Nationwide normative data were collected from 7,166 students from grade 1 to 7 over the district of Taiwan, and its mean (±SD) was 50 ± 10 (29).

<sup>b</sup> Case number of those whose scholastic performances were below the 10th percentile of the school class.

<sup>c</sup> Case number of whose rating scales were <2 standard deviations from the mean.

<sup>d</sup>  $p < 0.05$ .

12.6% (11:87) in FC group and 9.2% (8:87) in CC group. Again, there was no significant difference in every aspect of the behavior problems between these two groups (Table 1).

### Differences in neurocognitive attentions between FC and CC groups

Regarding the error patterns in the five neurocognitive attention tasks, the total impulse errors and commission errors on all five tasks were comparable for FC and CC groups (Table 2). The FC group had significantly fewer total missing errors than the CC group ( $p < 0.005$ ). With regard to the different error patterns on different atten-

tional tasks, the FC group was characterized by significantly fewer missing errors than the CC group on searching task ( $p < 0.005$ ), go-no-go task ( $p < 0.01$ ), and principle reverse task ( $p < 0.01$ ). The FC group also had significantly fewer commission errors than the CC group on go-no-go with distracters ( $p < 0.05$ ). There were significantly fewer impulse errors in the FC group on the searching task ( $p < 0.01$ ). However, the FC made more impulse errors in the other four tasks than the CC group.

The FC group had faster hand motor speed than the CC group ( $329.23 \pm 5.07$  vs.  $348.96 \pm 7.86$  ms,  $p = 0.03$ ; Fig. 1). To adjust for the difference of hand motor speed and to calculate the speed of each cognitive process, the corrected mean reaction time (cMRT) for simple reaction, searching, go-no-go and go-no-go with distracters tasks was calculated by subtracting the MRT from the preceding simpler task. The FC group had significantly longer cMRT on the task of simple reaction ( $p < 0.005$ ), and go-no-go with distracters ( $p < 0.05$ ), but had shorter cMRT on the searching task ( $p < 0.005$ ) than the CC group. The FC group also showed significantly less variability of hand motor speed than the CC group on the searching tasks ( $p < 0.005$ ) and go-no-go ( $p < 0.005$ ). When the attention mechanism was subgrouped into four component processes, the proportion of children with attention deficits for each of the four components was comparable for the FC and CC groups (Table 3).

### Risk factor for attention deficits within FC group

The risks for neurocognitive attention deficits associated with environmental, genetic, biologic, and FC factors were assessed by both univariate and multivariate analysis. The results showed that gender was the only significant risk factor for deficits in sensory selection and in response control ( $p < 0.05$ ). The associated odds ratios of female versus male were 0.3 (95% confidence interval, 0.01–0.9), and 0.0 (95% CI, 0.0–0.27), respectively. However, this finding would be eliminated after a correction for the multiple testing of data by Bonferroni's

**TABLE 2.** Comparison of the error patterns in different tasks of attentional functioning between febrile convulsion and control group

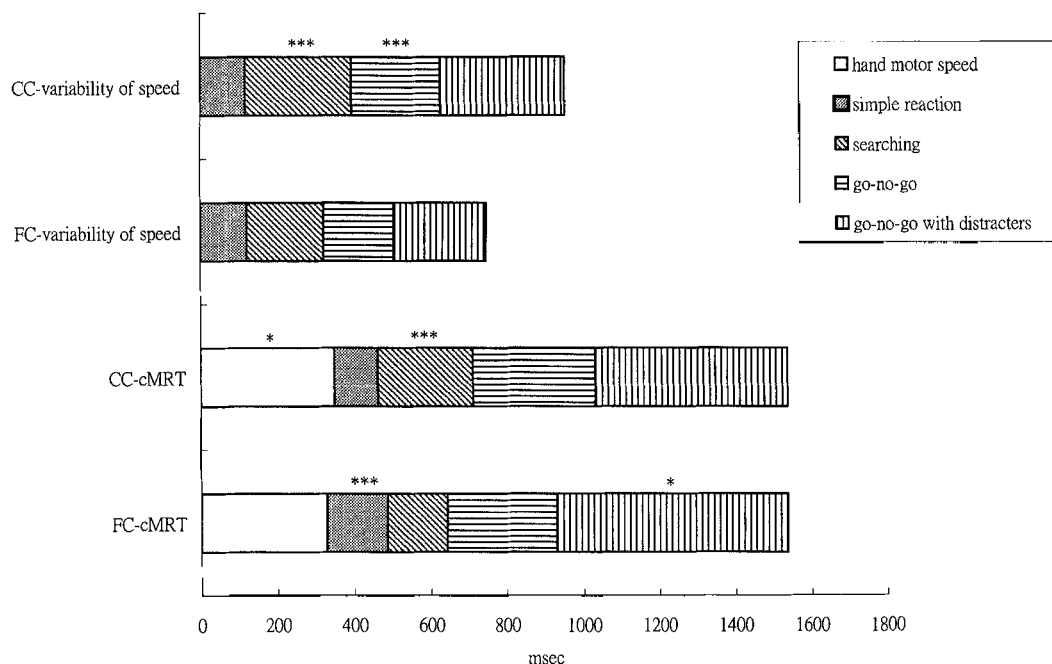
	Simple reaction task	Searching task	Go-no-go task	Go-no-go with distracters task	Principle reverse task	Total errors
Impulse errors						
FC group	1.25 ± 0.15 (87)	0.78 ± 0.13 (87) <sup>a</sup>	0.21 ± 0.06 (87)	0.48 ± 0.12 (87)	0.54 ± 0.16 (85)	3.19 ± 0.42 (85)
CC group	1.19 ± 0.16 (86)	1.25 ± 0.19 (84)	0.19 ± 0.08 (87)	0.31 ± 0.07 (87)	0.25 ± 0.07 (87)	2.88 ± 0.33 (83)
Missing errors						
FC group	0.18 ± 0.05 (87)	1.46 ± 0.22 (86) <sup>c</sup>	1.80 ± 0.19 (87) <sup>b</sup>	1.95 ± 0.20 (82)	0.63 ± 0.12 (87) <sup>b</sup>	5.95 ± 0.57 (81) <sup>c</sup>
CC group	0.24 ± 0.05 (87)	2.62 ± 0.23 (86)	2.64 ± 0.23 (81)	2.41 ± 0.21 (82)	1.30 ± 0.21 (86)	8.67 ± 0.66 (75)
Commission errors						
FC group			0.93 ± 0.13 (87)	1.10 ± 0.15 (86) <sup>a</sup>	0.57 ± 0.12 (87)	2.62 ± 0.27 (86)
CC group			1.28 ± 0.18 (85)	1.67 ± 0.20 (82)	0.56 ± 0.11 (86)	3.35 ± 0.34 (79)

The numbers in parentheses refer to the case numbers after excluding those who failed the task. Data are expressed as mean ± SEM.

Total errors, the sum of the errors in the task of simple reaction, searching, go-no-go task, go-no-go with distracters, and principle reverse task.

FC, febrile convulsion group; CC, control group.

<sup>a</sup>  $p < 0.05$ ; <sup>b</sup>  $p < 0.01$ ; <sup>c</sup>  $p < 0.005$ .



**FIG. 1.** The difference of corrected mean reaction time (cMRT) and variability of hand motor speed on different tasks between febrile convulsion group (FC) and control group (CC). \* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.005$ .

method. No significant risk factors for deficits in attention capacity and sustained attention were found. It was particularly noteworthy that characteristics of FC, such as onset of age ( $\leq 1$ , or  $>1$  years), presence or absence of complex FC, recurrent rate of FC ( $0, \geq 1$ – $\leq 3$ , or  $>4$ ), presence or absence of subsequent unprovoked seizures, prior use of anticonvulsants (yes or no), and seizure-free duration ( $\leq 1$ ,  $>1$ – $\leq 3$ , and  $>3$  years) was not associated with any of the neurocognitive attention deficits in FC children.

## DISCUSSION

This article summarizes the first population study to assess the different subcomponents of neurocognitive attention in school-age children with a history of FC. Most outcome studies on FC have emphasized the rate of FC recurrence and subsequent epilepsy (1–4,32,33). Some studies measured the behavior and cognition outcome globally by scholastic achievement, intelligence tests, and behavioral questionnaires (6,7,10–15). The results were contradictory and conflicting (1–5). Few investigators focused on neurocognitive attention. This study used a timed neuropsychological battery to detect specific changes in neurocognitive attention. In addition, our population-based case–control study is more representative of the neurocognitive outcome of FC children than are hospital-based studies, which may include the more severe and possibly atypical patients (5,10,11).

The timed neuropsychological battery allows a direct assessment of the major components of neurocognitive

attention (28,31). These results provide evidence that the neurocognition of school-aged children with a history of FC is characterized by a good control of distractibility and inattention, with, however, a nonsignificant trend of impulsivity. When the task was monotonous (i.e., simple reaction task), FC children had impairments in maintaining vigilance. However, they performed better on more difficult tasks (i.e., the go–no–go task, the go–no–go task with distracters, and the principle reverse task). The variability of hand motor speed, missing errors, commission errors, and total errors of these complex tasks in the FC group was significantly less than that in the CC group,

**TABLE 3.** Deficits in different components of neurocognitive attention between febrile convulsion and control children: comparisons of the number of subjects<sup>a</sup>

Deficits in neurocognitive attention	FC group (n = 87)	CC group (n = 87)	p Values
Sensory selection deficits	n = 30	n = 29	0.87
Simple focus attention	19	16	0.71
Searching skills	6	11	0.31
Filtering skills	7	9	0.79
Response control deficits	n = 17	n = 17	1.00
Impulsivity	14	10	0.51
Inhibitory control	4	11	0.16
Attention capacity deficits	n = 10	n = 11	1.00
Sustained attention deficits	n = 13	n = 15	0.68
Short duration	8	8	1.00
Relatively long duration	6	9	0.40

FC, febrile convulsion; CC, control.

<sup>a</sup> Case number of those whose attention errors were greater than 10th percentile of control or those who failed that task were defined as deficit in that attention component.

although at the cost of prolonged mean reaction time. These findings suggest that the executive function, including goal selection, plan formulation, selective attention, and cognitive flexibility in FC children is superior to that of the control children (19,28). The neurocognitive attention deficits in FC children thus may be based more on impulsivity alone rather than on the global disruption on the regulatory role. This is in accordance with other population-based studies showing an optimistic outcome in FC children (10–13).

Up to 30% behavioral disturbance has been reported among FC children in hospital-based studies (9,34). Only two prospective population-based studies have evaluated the behavioral outcome (10,14). Mothers of FC children reported more psychological disturbance and anxiety in their children than did mothers of control children, but there were otherwise no significant reported differences with respect to inattentiveness, hyperactivity, or conduct problems (10,14). The FC children also did not differ from the control on teachers' behavioral ratings (10,14). In agreement with the findings from other population studies (10,14), we found that FC children do not have disadvantages in behavioral outcome at school age, measured by both teachers' and parental ratings. Specific learning difficulties, including drawing and arithmetic, have been reported in FC children in hospital-based studies (7,35). In contrast, other population studies (10,15) as well as ours have demonstrated that FC and control children have comparable scholastic performance. Moreover, we found that the FC children had significantly higher scores on the Chinese Achievement Test than did the CC group. This finding may be due to the fewer missing errors and commission errors demonstrated by the neurocognitive attention test in FC children. These results further extend and reassure the favorable outcome of the FC children.

One prior study evaluated sustained attention on continuous performance tests of 15 FC children in a referral hospital. In contrast to our study, Hara et al. (24) found significantly higher omission errors and commission errors in FC children than in control children. The difference in patient selection may be one of the reasons for the different results, because population-based studies usually report better outcome than do hospital-based studies (5,10,11). The other reason may be the variability of task demands, novelty, and attractiveness of the test. The attention performance of children is in large part situation dependent (28,31). By measuring the performance on tasks with different levels of difficulty, we found that FC children do have subtle difficulty sustaining their attention on simple tasks but not on more complex tasks.

Although no overriding theory yet exists to integrate all the subcomponents of neurocognitive attention within

a unifying framework, several models have been proposed and indicate that different attentional processes are localized in different neuroanatomic sites or systems (36–38). The posterior attention network is involved in the orientation to sensory stimuli. It includes a portion of the parietal cortex, a part of the thalamic area of the pulvinar and reticular nucleus, and part of superior colliculus in the midbrain. The anterior attention network, including the mid-prefrontal cortex, involves executive function (38). Patients with lesions in the medial frontal lobe in either hemisphere make more commission errors (39). The anterior cingulate cortex is generally involved in selective attention (40). There is evidence that the prefrontal cortex plays a key role in response selection for attention control (31). For sustained attention, studies point to a critical involvement of the frontal and parietal cortex, irrespective of the modalities (41). There seems to be a tendency for vigilance and impulsivity to be right frontal lobe related (38,40). Further study is needed to find out whether the better executive function and non-significant trend of impulsivity in FC children is frontal lobe related.

Current literature has very few outcome studies that delineate the risk factors associated with neurocognitive disadvantage in FC children (10,12,34,42). The National Collaborative Perinatal Project in United States found that the neurologic or developmental abnormality predated FC, and subsequent afebrile seizures were the important predictors of intellectual impairment (12). The Child Health and Education Study in the United Kingdom reported that those who had FC in the first year of life required more special schooling than did those who had FC later in life (10). We found, however, that these risk factors did not influence the attention functioning of FC children. Although complex FC is known to be associated with subsequent epilepsy, its effect on intellect is a matter of current dispute. It has been shown that children with prolonged or recurrent FC perform more poorly in mental performance in hospital-based studies (34,42). In our study, complex FC, recurrent FC, or subsequent unprovoked seizures were found to have no adverse effect on attention, which is consistent with other population-based studies (10,12). It implied that the attention deficit among FC children might not related to the seizure per se.

Although there is a high rate of FC recurrence, the long-term outlook for FC children is favorable and optimistic (10–13). Neuroimaging and neuropathologic studies, however, have demonstrated an association of mesial temporal sclerosis and complex FC in early childhood (16–18). In most patients with complex partial seizures, the preceding FCs were complicated (i.e., prolonged, focal, recurrent, or occurring at a young age) (41). It is still unclear whether it is due to the detrimental

effects of seizures or preexisting minor cerebral abnormalities (11). Our study seems to indicate that there is subtle neurocognitive dysfunction in school-age children having previous FC, although the global outcome is favorable. This dysfunction, however, does not correlate with complex FC, recurrent FC, and subsequent unprovoked seizure. A larger scale population and long-term follow-up study may be needed to delineate the pattern of neurocognitive dysfunctions and their associated risk factors among FC children.

Our CC group came from a nationwide sample among school-age children attending regular classes selected according to the characteristics of urbanization level in Taiwan districts by probabilities proportional to size method (28). The CC group consisted of 87 children from this nationwide sample age-matched to the children in the FC group by individual. Each of the age-matched controls was selected by using a random number table from the age-matched nationwide sample to each child in the FC group. It turned out that 10% of the children in the CC group had scholastic problems, as we had expected from the use of 10th percentile of normative data for ascertainment. In addition, the proportion of children with scholastic difficulties was similar between FC group and CC group. Moreover, the age-matched CC group did equally well on the Chinese Achievement Test (mean  $\pm$  SD,  $48.5 \pm 1.1$ ) as compared with the nationwide normative data in the same age range (mean  $\pm$  SD,  $50 \pm 10$ ) (29). Therefore we believe that the CC group was not a selective subgroup of the nationwide sample. There was also no significant difference in the parents' socioeconomic status between the FC and CC groups, so the FC group did not come from families with higher intellectual abilities. It seems unlikely that the better score on the Chinese Achievement test and fewer missing errors and commission errors by neurocognitive attention test in the FC children was attributed to the difference in social and demographic background. Both the FC and CC groups were representative of their populations, and the differences were unlikely to be due to selection biases.

This study is happily able to reassure parents about the favorable prognosis of FC. This study found that FC is not associated with a decrement in neurocognitive attention, early academic performance, or behavioral outcome. Surprisingly, and in contrast with previous studies that showed no difference, this study found that FC children demonstrated significantly better control of distractibility and attention. Further study is needed to examine the underlying mechanisms that make a child more prone to FC and also more attentive.

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