



Less efficient and costly processes of frontal cortex in childhood chronic fatigue syndrome



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ABSTRACT

The ability to divide one's attention deteriorates in patients with childhood chronic fatigue syndrome (CCFS). We conducted a study using a dual verbal task to assess allocation of attentional resources to two simultaneous activities (picking out vowels and reading for story comprehension) and functional magnetic resonance imaging. Patients exhibited a much larger area of activation, recruiting additional frontal areas. The right middle frontal gyrus (MFG), which is included in the dorsolateral prefrontal cortex, of CCFS patients was specifically activated in both the single and dual tasks; this activation level was positively correlated with motivation scores for the tasks and accuracy of story comprehension. In addition, in patients, the dorsal anterior cingulate gyrus (dACC) and left MFG were activated only in the dual task, and activation levels of the dACC and left MFG were positively associated with the motivation and fatigue scores, respectively. Patients with CCFS exhibited a wider area of activated frontal regions related to attentional resources in order to increase their poorer task performance with massive mental effort. This is likely to be less efficient and costly in terms of energy requirements. It seems to be related to the pathophysiology of patients with CCFS and to cause a vicious cycle of further increases in fatigue.

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1. Introduction

Up to 8% of children and adolescents have experienced fatigue for a duration of more than 1 month, and nearly 2% have experienced chronic fatigue lasting more than 6 months (Miike and Bell, 2008). Because fatigue in students corresponds to a decrease in academic performance (Garralda and Rangel, 2002), clarification of the precise mechanisms of fatigue and identification of ways to overcome fatigue are very important. Fatigue induces difficulty in initiating or sustaining voluntary activities (Chaudhuri and Behan, 2004). In fact, fatigued children and adolescents and patients with childhood chronic fatigue syndrome (CCFS), which is characterized by profound and disabling fatigue for

6 months (Fukuda et al., 1994), show poor performance on cognitive tasks related to memory and attention (Haig-Ferguson et al., 2009; Kawatani et al., 2011; Mizuno et al., 2013a; Tomoda et al., 2007).

Along with structural changes in the brain from childhood to adolescence, executive function, defined as the set of mental cognitive control processes that permit goal-directed behavior, develops dramatically between childhood and adolescence (Travis, 1998). Recently, we reported that task performance on a divided attention task using the Kana Pick-out Test (KPT), which assesses participants' allocation of attentional resources to two simultaneous activities [picking out vowels (PV) and reading for story comprehension (SC)] improved as children progressed from elementary to junior high school (Mizuno et al., 2011a), and decreased with fatigue (Mizuno et al., 2011b) and lower academic motivation (Mizuno et al., 2011c). Poor performance of the KPT also relates to poor lifestyle choices (skipping breakfast, too much time watching television) and family conditions (little time spent with family and little praise from family members) in junior high school students (Mizuno

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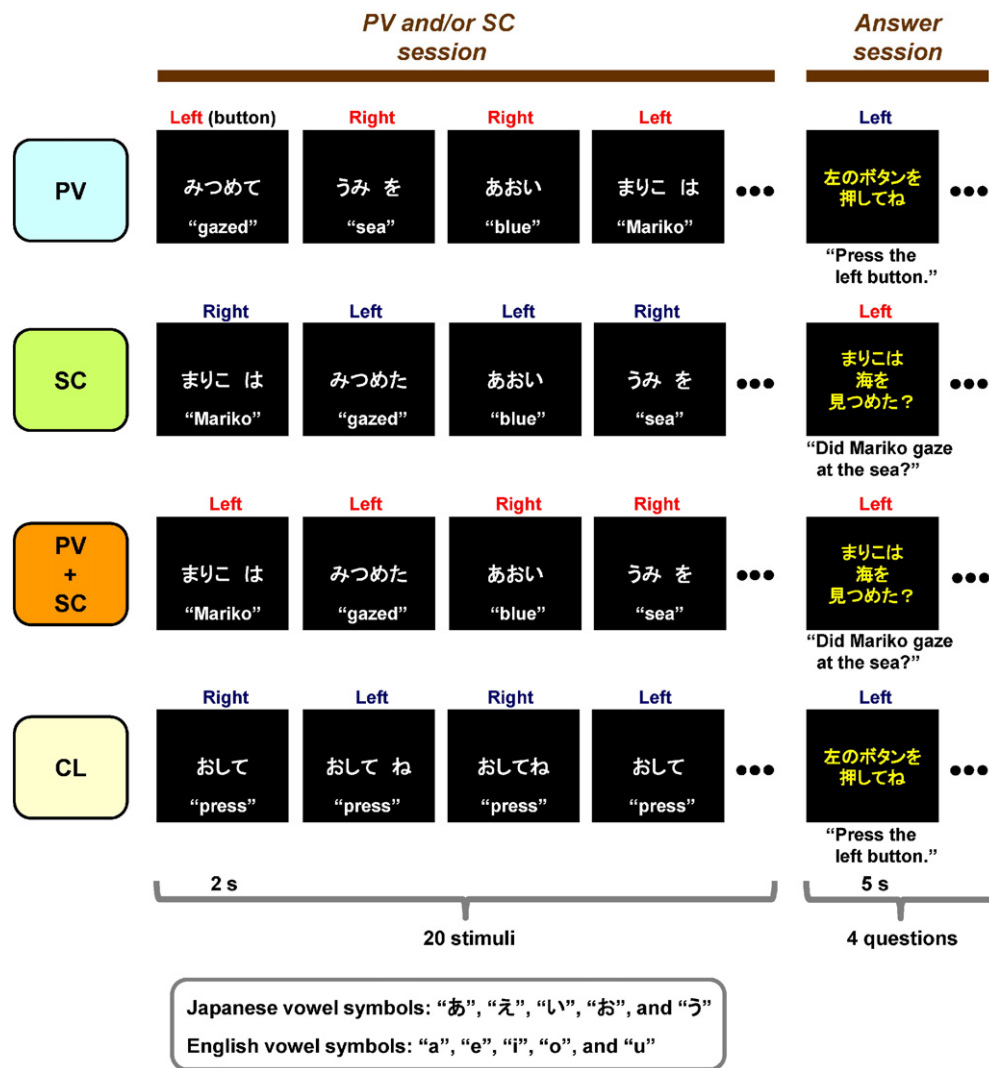


Fig. 1. Time course of stimulus display sequences. The PV and/or SC session involved picking out vowels (PV), story comprehension (SC), the concurrent processes of both PV and SC (PV + SC) and control (CL) conditions. In the PV condition, participants judged whether a target word included vowels (/a/, /e/, /i/, /o/, and /u/). In the SC condition, participants read each word presented in sequence on the screen and were later tested for comprehension of the short story. In the PV + SC condition, participants concurrently performed both picking out vowels and story comprehension. In the CL condition, participants pressed either the right or left button in alternate trials. The word “press” appeared on the screen for every control trial. After the PV and/or SC session, participants completed an answer session. In the SC and PV + SC conditions, participants answered four questions, designed to require “yes” or “no” answers. Although the Japanese version of the task was used in the present study, an English version was also developed.

et al., 2013b). CCFS patients also have lower performance on the KPT (Tomoda et al., 2007). These findings suggest that although development of the ability to divide attention is crucial for good academic

performance in adolescence, it is inhibited by fatigue, not only in healthy children and adolescents (HCA), but also in CCFS patients. Therefore, clarifying the neural relationship between fatigue and

Table 1
Demographic characteristics of participants.

	HCA				CCFS
	1st trial	2nd trial	3rd trial	All	
Age (years)	12.2 ± 0.8	13.5 ± 0.9	14.4 ± 0.9	13.4 ± 1.2	13.5 ± 1.0
BMI (kg/m ²)	18.6 ± 1.7	19.6 ± 2.3	20.2 ± 2.2	19.5 ± 2.1	20.1 ± 4.2
Disease duration (month)					12.3 ± 6.4
WISC-III, FIQ score					96.9 ± 12.2
Fatigue score	11.0 ± 6.3	12.4 ± 7.6	14.0 ± 9.2	12.5 ± 7.7	17.5 ± 6.1 [*]
VAS score for motivation					
CL	64.4 ± 27.1	71.8 ± 12.3	73.5 ± 19.7	69.9 ± 20.4	65.6 ± 15.9
PV	68.1 ± 20.5	71.5 ± 14.4	78.8 ± 13.4	72.8 ± 16.6	61.3 ± 19.5
SC	66.4 ± 25.4	70.3 ± 16.8	75.6 ± 10.7	70.8 ± 18.5	66.8 ± 15.3
PV + SC	61.5 ± 28.1	68.0 ± 21.5	78.8 ± 24.7	69.5 ± 25.3	61.0 ± 22.0

HCA, healthy children and adolescents; CCFS, childhood chronic fatigue syndrome; BMI, body mass index; WISC-III, Wechsler intelligence scale for children-third edition; FIQ, full scale intelligence quotient; VAS, visual analogue scale; CL, control condition; PV, picking out vowels condition; SC, story comprehension condition; PV + SC, concurrent processes of PV and SC conditions. Values are the number or mean ± SD.

^{*} $p < 0.05$, significantly different from the corresponding values for the healthy adolescents (All).

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