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Cognitive dysfunction accompanied by neurofibromatosis type 1 is one of the significant characteristics of this neurocutaneous disorder and has a serious impact on patients' quality of life. Although studies on cognitive function in children with neurofibromatosis type 1 have revealed that attentional impairment is a key deficit in these patients, few studies have examined their neuropsychological profile, especially whether the attentional function is also abnormal and specific in adult patients with neurofibromatosis type 1. In this study, <sup>Diseases,</sup> we used the revised attention network test to examine the function of three attentional networks—alerting, orienting and executive control—in 20 adult patients with neurofibromatosis type 1 in comparison to 20 normal controls. Adult patients with neurofibromatosis type 1 showed significant greater conflict effect for the executive control network, but no significant differences were found for alerting and orienting network relative to normal controls. These results provide evidence that there is an attentional deficit which is specifically associated with the executive control network in adult patients with

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networks, including the ability to maintain alertness, the ability to orient the sensory input and perform control functions [13]. Identification of the general or selective impairments in attention in adult patients with NF1 would enable us to understand higher-level functional deficits in this population. This study sought to determine whether adult patients with NF1 have attentional impairment and, if so, to clarify the profile of attention

72 trials in each block. The total time required to complete the task is approximately 30 minutes, which is suitable for studies of patients. The experimental program was presented in E-prime (Psychology Software Tools, Pittsburgh, Pennsylvania, USA). Participants' reaction time (RT) and accuracy were recorded.

#### **Data analysis**

The effects of the attentional networks in ANT-R were compared between the NF1 group and the HC group to reveal the networks might be functioning abnormal in NF1 patients. The scores of each of the three networks in ANT-R were calculated according to the previous study [17]. Incorrect responses were excluded from the computation of the mean RTs. The effects in RT and accuracy were entered into repeated-measures analysis of variances (ANOVAs), with attentional network (alerting, orienting or executive control) as the within-subject factor and group (NF1 and NC group) as the between-subject factor. In addition, we calculated Bayes factors (BFs) with a Cauchy prior distribution to determine the relative

of attention in adult NF1 patients, but no evidence of deficits in alerting and orienting functions.

#### **C** *Behavioral characteristics*

The NF1 patients fulfilled the diagnostic criteria as specified by the NIH Consensus Development Conference [20]. All patients had small benign subcutaneous nodules or café au lait spots on the trunk and extremities; these skin features did not affect normal activities. The patients were in stable clinical situation and could go about their work and daily activities independently. The patients had not undergone surgery and had no serious diseases that affected their quality of life (such as scoliosis and other osseous lesions). All patients had normal MMSE scores (score  $28.9 \pm 0.7$ , out of 30, Table 1), while their BDI scores showed moderate depressive symptoms (score  $9.8 \pm 2.9$ ). None of the patients showed any dysfunction on routine neurological examination.

#### **D** *Discussion*

##### **I** *Attention and attentional functions in NF1*

Attention and attentional functions (i.e. the alerting, orienting, and executive control functions) are supported by independent and integrative brain networks [13]. The ANT-R tests these three functions of the attention network in a single task, making it possible to use one test to simultaneously evaluate the three functions of the attention network and to study the interaction of the three subnetworks [17]. However, there has been controversy about the efficiency of these three networks acting on human attention and the interactions between them. The previous literature on attention deficits in NF1 patients (mostly focussed on children) does not explicitly show which specific domain of attention has abnor-

deficit in behavioural inhibition results in executive deficits that depend on this inhibition.

### Cognitive deficits in children with NF1

Cognitive deficits in children with NF1 were first identified as a problem due to poor academic performance. Some children with NF1 also showed deficits on intelligence tests, and their scores were significantly lower than those of healthy children of the same age. Most children with NF1, even if their mental development is fundamentally normal, have complex cognitive impairments affecting perception, executive function and language skills; these impairments cause learning difficulties, which constitute the main symptom of NF1. At the same time, 40% of children with NF1 show ADHD-like performance deficits [22], such as executive control disorder, planning choice ability defects and learning defects, which seriously affect their ability to develop and pursue an education. In addition, increasingly many studies have noted that various types of cognitive damage last throughout the lifespan. For adolescents with NF1, symptoms such as impaired motor development, visual-spatial judgment and visual-motor integration suggest that NF1 may affect multiple stages of cognitive processing [12]. In an overall cognitive assessment of elderly patients with NF1, a mild intelligence deficit was found, and short-term memory showed a significant decline, confirming that cognitive dysfunction is persistent and evolving in the progression of NF1 [10]. Generally, the cognitive impairments caused by NF1 are multidimensional phenomena that involve several psychological processes, moreover, all of these processes are related to executive control of attention which is the key process associated with the NF1's decline in cognitive abilities.

### Pathways of cognitive impairment in NF1

Cognitive processing by the brain is based on a complex neural network involving multilevel regulatory mechanisms. The mechanisms that cause NF1-associated cognitive impairment include molecular and cellular signalling pathways, neuronal differentiation and many other complex factors [9], the most important of which are the roles of neurotransmitters and neuronal activity.

Abnormalities in local brain activation and structure of the whole brain network

In recent studies of brain functional status and structures using new neuroimaging techniques, NF1 patients demonstrated enhanced connectivity of the default-mode network [8] and abnormal activation of the visual cortex

