Cognitive impairment in patients with carotid artery occlusion and ipsilateral transient ischemic attacks

Abstract Although transient ischemic attacks (TIAs) by definition do not cause lasting neurological deficits, cognitive impairment has been suggested in patients with carotid artery disease who have suffered from a TIA. The purpose of our study was to assess whether patients with carotid artery disease and TIAs are cognitively impaired, to describe the frequency, nature and severity of this impairment, and to search for associated patient characteristics.

Thirty-nine consecutive patients with carotid occlusion and ipsilateral cerebral or retinal TIAs, and 46 healthy controls underwent extensive neuropsychological assessment. Performances were compared group-wise with analysis of variance. In addition, the presence of cognitive impairment in the individual patient was determined. Associations between illness characteristics and cognitive impairment were explored with regression analysis.

Fifty-four percent of patients were cognitively impaired. Cognitive deficits were non-specific in nature and mild in severity. Impairment occurred also in patients with isolated retinal symptoms and in those without visible ischemic brain lesions on MRI. Neither the presence of any vascular risk factor, the side of the symptomatic carotid occlusion, the uni- or bilateral nature of carotid occlusion, nor the number of cerebral ischemic lesions were predictors of cognitive impairment.

We conclude that about half of the patients with carotid artery occlusion and ipsilateral TIAs are cognitively impaired. The presence of cognitive deficits in patients with isolated retinal symptoms and in those without cerebral ischemic lesions on MRI argues against an exclusive role for structural brain damage in the pathogenesis of these deficits.

Key words cognition disorders · carotid artery disease · transient ischemic attack

Introduction

In patients with transient ischemic attacks (TIAs) associated with stenosis or occlusion of the carotid artery, by definition no neurological signs of the TIA remain after 24 hours. Yet, subtle cognitive deficits have been reported up to months after the event [3]. These deficits may be caused by structural brain damage or by chronic compromise of the cerebral blood flow [22, 35].

There is controversy with respect to the occurrence and, if present, the extent of cognitive impairment in patients with carotid occlusive disease [3]. Insufficient information about the neurological deficits of patients and methodological flaws preclude a conclusion to this debate. Most studies did not give information about the
degree of stenosis, or the number and location of ischemic brain lesions. Moreover, cognitive functioning has been examined mainly in a selection of patients with carotid occlusive disease, i.e. patients suitable for carotid endarterectomy or extracranial intracranial (EC/IC) bypass surgery [3]. The aim of the current study was to assess the prevalence, nature and severity of cognitive impairment in patients with carotid artery disease who have suffered from a TIA. In addition, we investigated which illness characteristics were associated with cognitive impairment. We sampled patients with a symptomatic occlusion of the carotid artery, as these may be at the highest risk of a compromised cerebral blood flow.

**Methods**

**Patients**

Thirty-nine patients with symptoms of transient (lasting less than 24 hours) ischemia attributable to an occlusion of the carotid artery were recruited from consecutive patients referred to the outpatient clinics of the departments of Neurology or Vascular Surgery of the University Medical Center Utrecht, The Netherlands. Symptoms should have occurred within six months prior to inclusion in the study. All patients received angiography to confirm the carotid artery occlusion. Excluded were patients with a stroke within six months prior to inclusion, and patients with a modified Rankin grade [4] of more than three. The degree of stenosis in the contralateral carotid artery was measured on digital subtraction angiograms according to the NASCET criteria [9]. All patients underwent magnetic resonance imaging (MRI) to assess the presence of infarcts and ischemic white matter lesions [39] in the symptomatic and asymptomatic hemisphere (1.5-Tesla whole body system, ACS/NT-15 model, Philips Medical Systems, Best, The Netherlands, sagittal T1-weighted spin-echo sequence and T2-weighted spin echo) and were interviewed and investigated for the presence of vascular risk factors. Handicap was assessed by means of the modified Rankin scale [4].

The median time interval between the last ischemic event and the MRI and neuropsychological examinations was 50 and 54 days, respectively (range: two days to six months, 13 patients with symptoms less than 3 months ago). In each patient, all investigations were done within a few days.

**Controls**

Spouses, and occasionally siblings, of the patients were asked to cooperate with the study, thus providing a healthy control group. Excluded were persons with neurological or psychiatric diseases.

**Neuropsychological assessment**

Patients and controls underwent an identical, comprehensive neuropsychological assessment. The tests, ordered according to the measurement pretensions, and the parameters used for data analysis are listed below. Patients were screened for the presence of dysphasia, agnosia or apraxia. Signs of these disorders in executing the tests, in making conversation, or in moving around were recorded and, if present, further explored by means of a picture-naming and a writing task in case of dysphasia, and a drawing task in case of unilateral neglect [34]. Patients’ spouses were interviewed with respect to changes in patients’ everyday cognitive functioning.

**General Intelligence**

Nonverbal intelligence was assessed with the Standard Progressive Matrices (SPM) [28]. We used a time limit of twenty minutes, and scored the number of correct answers (maximum = 60). In addition, we performed the Vocabulary subtest of the Wechsler Adult Intelligence Scale (WAIS)-Revised [41], which is relatively insensitive to brain damage [45], and yields an indication of premorbid verbal intelligence. The maximum score is 70.

**Learning and Memory**

Of the Wechsler Memory Scale Form 1 (WMS) [40], we used the raw score with a maximum of 97. The Verbal Learning and Memory Test (VLMT) [25] is the recently developed Dutch version of the California Verbal Learning Test [8]. The reproductions of a list of sixteen orally presented nouns were summed over five trials (maximum = 80). Of the Visual Retention Test part C, administration A (VRT) [32], we scored the number of errors.

**Executive function**

Of the Trail Making Test (TMT) [30], we used the number of errors (part A and B) and the increase in execution time from part A to part B. Of the Modified Card Sorting Test (MCST) [26], we scored the number of errors. In the Word production according to lexical rules (UNKA-test) [17], a production time of 60 seconds per phoneme was used and the total number of correct words was counted.

**Reaction speed**

In the “simple” conditions of the Vienna reaction apparatus [31], sequences of single stimuli were presented (a yellow light and a tone, respectively). The third and fourth conditions were of the go-no go type; combinations of stimuli were presented among irrelevant signals that had to be ignored. In each condition, the median reaction time (ms) was calculated, and its components (median decision and median motor time).

**Motor speed**

The Tapping task [31] is a measure of motor speed, and is as such not a cognitive task. Nonetheless, this task is useful for the interpretation of performance on other tasks. Manual paresis or clumsiness, as observed on the tapping task, can have an adverse impact on the manual responses in the execution of cognitive tasks. The number of taps was counted for each hand.

**Mood**

The VROPSOM [38] is the Dutch version of the Depression Adjective Check Lists [23, 42], which screen for the presence of depressive affect. The score was the sum of dysphoric items ticked and euphoric items not ticked.

**Data analysis**

The characteristics of patients, controls and subgroups of patients were compared with an analysis of variance (ANOVA) (age), the Mann-Whitney U test (education, profession [33]) and the Chi-square or Fisher’s exact test (sex, presence of vascular risk factors, angiographic and MRI findings).

**Case-by-case**

To determine whether cognitive impairment was present on an individual level, we used a cut-off point for impairment on each task. In choosing the cut-off points, we relied as much as possible on psycho-