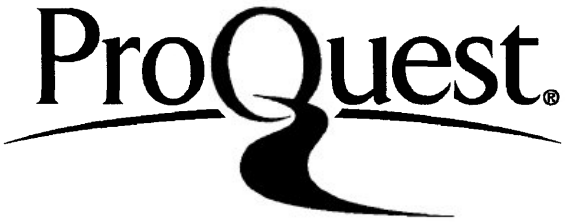
A Further Investigation of Cognitive Impairment in Migraine Subjects

Deborah E. Anderson ©

Department of Psychology

Lakehead University



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Abstract

The objective of the present study was to further investigate the hypothesis that repeated migraine attacks may cause permanent and possible cumulative neurological damage involving higher cortical functions (Zeitlin & Oddy, 1984; Hooker & Raskin, 1986). Previous empirical research has found evidence both in support (Zeitlin & Oddy; 1984, Hooker & Raskin; 1986) and contrary to this hypothesis (Leijdekkers, Passchier, Goudswaard, Menges & Orlebeke; 1990). In the present study, fourteen migraine with aura, fifteen migraine without aura and twelve control subjects from the community participated. They were manually-administered a two-hour neuropsychological battery which included tests used in the previous studies. This study found no evidence to support the hypothesis of permanent cognitive impairment in migraine subjects. In addition, no significant correlations between headache history or severity and performance were found for those subjects who had a minimum of two test scores in the impaired range. Therefore, there is no evidence to support the hypothesis that repeated migraine attacks may cause cumulative cognitive deficits.

A Further Investigation of Cognitive Impairment in Migraine Subjects

Migraine headaches affect 23-29 per cent of women and 15-20 percent of men (Waters & O'Connor, 1975; as cited in Zeitlin & Oddy, 1984). Of all migraine sufferers, 10 percent of these people suffer from classic migraine (Edmeads, 1982). Presently, migraine is considered to be an essentially benign disorder (Leijdekkers, Passchier, Goudswaard, Menges & Orlebeke, 1990). It is thought that the neurologic dysfunction of the migraine attack is transient and usually completely reversible (Hooker & Raskin, 1986). However, complications related to severe migraine (incidence of 1.2 - 3.8 per cent according to Heyck & Krayenbuhl, 1964; as cited in Zeitlin & Oddy, 1984) have been documented since the 19th century (Gruber, 1860; Charcot, 1890; as cited in Zeitlin & Oddy, 1984; and Fere, 1881; as cited in Carroll, 1968, for example). Although the clinical symptoms clear after an attack there is some evidence which suggests that there may be permanent and possible cumulative neurological damage involving subtle higher cortical

functions (Zeitlin & Oddy, 1984; Hooker & Raskin, 1986).

To facilitate research and diagnosis of headaches, the National Institute of Neurological Diseases and Stroke, in 1962, formed an Ad Hoc Committee to classify the various kinds of headaches; they listed 15 major and 14 minor types (Journal of the American Medical Association, 1962). They classified migraine as: "a vascular headache involving the dilation of some blood vessels in the head and the constriction of others, as well as a host of other biological reactions throughout the body that accompany the head pain." A few years following this, the Research Group on Migraine and Headache of the World Federation of Neurology (1969) agreed upon this definition of migraine: (Journal of the Neurological Sciences, 1969)

> "A familial disorder characterized by recurrent attacks of headache widely variable in intensity, frequency and duration. Attacks are commonly unilateral and are usually associated with anorexia, nausea and vomiting. In some cases they are preceded by, or associated with, neurological and mood

disturbances. All the above characteristics are not necessarily present in each attack or in each patient".

Vascular headaches of the migraine type have been subdivided. The following are classifications by Edmeads (1982) and are used most frequently by headache specialists and researchers. "Common" migraines are headaches believed to be produced by dilatation and increased pulsation of the arteries of the scalp and face. They may be either unilateral or bilateral. Pain is characteristically throbbing and sharp in nature and usually not as intense as classic migraine; pain begins more gradually than classic migraine. Common migraine is often accompanied by nausea and sometimes vomiting, photophobia (intolerance to light), hyperacusis (abnormally acute hearing), chilliness and polyuria (excessive secretion of urine). During headaches there may be detectable distension and tenderness of scalp arteries. Compression of the affected artery may transiently ease the pain by collapsing it distally - this suggests the headache comes from distended extracranial vasculature. "Classic" migraines are characterized by an aura in

which decreased cerebral blood flow with cortical ischemia precedes the extracranial vasodilation. The aura symptoms vary and include such things as visual disturbances (bright, jagged lines, flickering obcurations, field defect distortions), hemiparesis (musculature weakness or partial paralysis restricted to one side of the body), numbness and dysphasia (loss or deficiency in the power to use or understand language). The aura typically lasts 10 - 30 minutes and is replaced by a throbbing, pulsing headache often accompanied by nausea and the other related migraine symptoms. Pain is usually unilateral in a classic migraine.

The most recent classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain was produced in 1988 by the Headache Classification Committee of the International Headache Society (Cephalalgia, 1988). The terms "classic" and "common" migraine were replaced by "migraine with aura" and "migraine without aura" to provide more information and decrease confusion. The term "aura" refers to the complex of focal neurological symptoms which initiates or accompanies a migraine attack. Premonitory

symptoms, usually consisting of hyperactivity, hypoactivity, depression, craving for special foods, repetitive yawning and similar atypical symptoms, occur hours to a day or two before a migraine attack (with or without aura). The terms previously used such as prodromes and warning symptoms, often synonymous with aura, should no longer be used.

Evidence Suggestive of Permanent Neurological Damage

Symonds (1952) described a 52 year-old man who suffered from complicated migraines, whom he had observed over three severe attacks. This patient's father had suffered similar severe attacks from a young age, often requiring hospitalization. Repeated attacks of hemiplegia were associated with cumulative dementia, and eventually led to the father's admission to a mental hospital. In the assessment of his patient, Symonds (1952) noted that there was a gross disorder of function in the EEG which rapidly returned to normal. In addition, a polymorphonuclear pleocytosis was found in the cerebrospinal fluid. Symonds (1952) suggested that slight, but cumulative, structural damage as a result of repeated attacks was plausible, based on the

latter finding and the dementia in this patient's father.

In 1962, Connor described a number of cases in which retinal, cortical and brain-stem lesions had occurred. He indicated that the evidence in his cases were very suggestive in implicating migraine as the cause of the lesions but that this was impossible to prove. Most of the cases were well below the usual age of onset for cerebrovascular disease, and all other causes of cerebrovascular accident had been ruled out. Nine cases of the eighteen developed lesions during a migraine attack and nine developed permanent damage in the areas of the body in which a temporary loss of function had previously been experienced.

Carroll (1968) described a number of cases in which permanent visual defects (hemianopia, field defects) were suffered by 7 migraine patients.

A patient described by Lohlein (1922, as cited in Zeitlin & Oddy, 1984), completely lost sight in the eye in which repeated retinal haemorrhages occurred during migraine attacks.

More recently, a number of researchers have found abnormalities in the CT scans of migraine samples (7 ·

59 per cent) (Mathew et al, 1977; Sargent et al., 1979; Hungerford et al., 1976; Cala & Mastaglia, 1980; as cited in Zeitlin & Oddy, 1984). The scans indicated diffuse and localized cortical atrophy most frequently in the temporal and parietal regions and cerebral parenchymal low density areas. These studies were unable to address the significance of these findings however, as norms for the incidence of CT scan abnormalities in the general population were unavailable.

Mathew et al. (1977, as cited in Zeitlin & Oddy, 1984) also postulated that migraine attacks may cause cumulative damage. This hypothesis was based on their findings of cortical atrophy in three patients who suffered severe frequent attacks.

Cohen & Taylor (1979, as cited by Zeitlin & Oddy, 1984) found areas of old and new cerebral infarction in a 32 year-old man who suffered basilar artery and hemiplegic migraine. They noted this evidence was circumstantial but that there were no other identifiable causes of cerebral infarction.

Two studies also reported intellectual deficits in a small number of cases. Connor (1962, as cited by

Zeitlin & Oddy, 1984) found intellectual deterioration in 2 patients with cortical lesions; these lesions were thought to be directly related to their severe migraine attacks. Pederson (1980, as cited by Zeitlin & Oddy, 1984) found marked signs of reduced intellect in 3 patients with cortical atrophy. For two of these patients, there was an increase in frequency of migraine attacks just prior to the onset of dementia. No other explanation for this change aside from the migraine attacks could be found. Pederson (1980, as cited by Zeitlin & Oddy, 1984) suggested cumulative cerebral anoxic incidents during the ischaemic phase of the migraine attack were responsible for the cortical atrophy.

Empirical Studies Investigating Permanent Neurological Damage

In 1984, Zeitlin and Oddy conducted a controlled study to further examine the earlier tentative evidence of permanent and possible cumulative neurological deficits associated with migraine. The hypotheses tested were:

1) that severe migraine, over a period of time,

results in detectable cognitive impairment measured by neuropsychological techniques

2) that the impairment is cumulative in nature and as such will be related to the severity of the individual's migraine

Their subject pool consisted of 19 subjects selected from patients attending a migraine clinic (both classic and common type) and a matched nonheadache control group. The subjects were administered a battery of tests which included tests selected on their likely sensitivity to minimal cognitive impairment and to cover different sensory modalities and cognitive functions. Subjects were also asked to fill out the Middlesex Hospital Questionnaire (MHQ), a self-report measure for psychoneurotic illness. The authors calculated two Severity Index measures based on each subjects' migraine history for duration, frequency, and years since onset. A drug history was also noted for the migraine patients. Zeitlin and Oddy (1984) found that migraine patients performed more poorly than the control group on all measures. The following five tests reached at least a five per cent level of significance: Trail-making A - (Halstead-Reitan

Neuropsychological Test Battery, (HRNTB), 1979), Reaction Time B and C - (Leeds Psychomotor Tester; Hindmarch, 1975; as cited in Zeitlin & Oddy, 1984), Paced Auditory Serial Addition Test (PASAT; Gronwall & Wrightson, 1974), and the Forced Choice test for words (National Hospital Forced Choice Recognition Test (Warrington & Ackroyd, 1975; as cited in Zeitlin & Oddy, 1984)).

The authors did not find a significant correlation between cognitive impairment and either of the two severity indices. Migraine patients were found to have significantly more somatic complaints, obsessionality and free-floating anxiety than the controls, as measured by the Middlesex Hospital Questionnaire. However, no significant correlation was found between any of the MHQ scales and the cognitive tests. No evidence was found to implicate ergotamine use as the cause of the cognitive deficits. Zeitlin and Oddy (1984) were unable to come up with an obvious or plausible explanation for their results. In their discussion they acknowledged some limitations of their study and made suggestions for further research. They hypothesized that the group differences in test

performance may be related to a personality or non-personality variable which differentiates migraine sufferers. They suggested their indices may not have sufficiently discriminated headache severity, as it is difficult to measure the subjective phenomenon of pain. Although they could not demonstrate a relationship between cognitive impairment and severity, they suggested cumulative neuropsychological damage was possible and required further study.

In 1986, Hooker and Raskin further investigated the hypothesis of cumulative neuropsychological impairment in migraine patients. They compared the performance of 16 classic and 15 common migraine outpatients with a matched nonheadache control group. In this study they specifically separated the migraine patients. The common migraine patients were used as a control for the influences of drug use, the psychologic stress attending episodic head pain as well as a control for the neurologic disturbance associated with classic migraine attacks. The subjects were administered a 2-3 hour neuropsychological battery consisting of measures of sensory-perceptual and motor skills, speech and language, verbal and nonverbal

reasoning and auditory and visual memory functions, many taken from established batteries. Subjects also completed a questionnaire assessing their own current functioning between migraine attacks. The authors calculated a number of measures; the Average Impairment Index was the mean of the scale scores from 11 tests shown to be especially sensitive to brain dysfunction, and a second impairment index was based on the percent of all tests with a scale score in the impaired range or with a raw score exceeding a pre-established impairment cut-off score. Headache frequency, duration, severity and drug use were also measured. In their analyses, Hooker and Raskin (1986) found that both classic and common migraine groups had significantly greater average impairment than the control group, but did not significantly differ between themselves. The three groups were not significantly different in the percentage of tests performed in the impaired range but there were a number of significant group differences. The classic migraine group alone performed significantly more poorly than the common migraine and control group on dominant and nondominant hand dexterity (Grooved Pegboard; HRNTB, 1979) and the

Aphasia Screening Test (HRNTB, 1979). They performed significantly poorer than the control group on dominant pure motor speed (Finger-tapping; HRNTB, 1979) and on the Digit Symbol subtest of the Wechsler Adult Intelligence Scale-Revised (Wechsler, 1981). The classic and common migraine groups together performed significantly more poorly than the control group on the Tactual Performance Test (dominant hand; HRNTB, 1979) and on long-term semantic verbatim memory (Wechsler Memory Scale; Russell, 1975). The common migraine group took significantly longer (total minutes) than the control group on the Tactual Performance Test (HRNTB, 1979). On examination of the Assessment of Own Functioning Questionnaire (Chelune, Heaton & Lehman, 1986), it was found that the classic migraine subjects reported significantly greater neuropsychologic dysfunction in their daily lives as compared to the control group. They indicated significantly more anomia, difficulties following directions and confused or illogical thought. Both classic and common migraine patients indicated significantly more problems in speech articulation, following instructions and understanding spoken speech as compared to the control

group. The authors discussed two classic migraine subjects with higher Average Impairment scores who were using two kinds of medication. Because this drug use could not be ruled out as affecting their performance, their scores were removed from the sample. Drug usage by the other subjects was not found to significantly interact with the Average Impairment Index. In their discussion, Hooker and Raskin (1986) noted that they did not expect the relative neuropsychologic impairment the classic and common migraine groups demonstrated because of the lack of a well-defined neurologic disturbance during a common migraine attack. Based on regional blood flow studies (Oleson et al., and Lauritzen & Oleson, as cited in Hooker & Raskin, 1986), research in which evidence for a neural pathogenesis of migraine was found (Blau, Pearce & Edmeads, 1984; as cited in Hooker & Raskin, 1986) as well as their behavioural data showing a moderate degree of overlap, the authors suggested that classic and common migraines may be on a continuum of pathophysiologic effects with classic migraine tending to fall at the more severe end of the spectrum.

In contrast with the preceding two studies,

Leijdekkers, Passchier, Goudswaard, Menges and Orlebeke (1990) found no significant differences in test performance between a migraine and control group on a neuropsychological battery. Their subject pool contained 37 female migraine patients (26 without aura, 11 with aura) and 34 healthy matched nonheadache controls. All subjects were given an intelligence test, two subtests of the WAIS-R (Wechsler, 1981) known to be sensitive to cerebral dysfunction (Block Design, Digit Symbol), an inductive reasoning test (Van de Vijver, 1988; as cited in Leijdekkers et al. 1990) and the Neurobehavioural Evaluation System (NES, a neuropsychological computer battery; Baker, Letz, Fidler et al. 1985). The NES was developed to test for subclinical deficits, particularly in the field of toxicology and is for use with a relatively healthy population. The authors selected basic behavioural tests rather than complex cognitive tests to control for background variables such as education and baseline intelligence level. In addition, subjects filled out several self-report questionnaires: Measurement of Invested Mental Effort (0 - 100), the State and Trait Anxiety Inventory (Spielberger, 1983), and the

Achievement Motivation Test (Hermans, 1976) (subscales: Achievement Motivation, Debilitating Anxiety, Facilitating Anxiety). Measures of headache frequency, duration, severity and drug use were recorded. Leijdekkers et al., (1990) calculated an overall impairment index reflecting the number of tests for which the score was greater than one standard deviation worse than the average score for the whole group; this was increased by the number of tests in which a score was more than two standard deviations worse than the average. They found no significant differences in cognitive performance or the impairment index for the migraine and control groups. Migraine with aura and migraine without aura subjects did not perform significantly different from the control group. No differences were observed between patients who used medication and those who did not. There was no significant correlation in the migraine group for length of headache history and cognitive impairment. In the self-report measures, migraine subjects reported significantly higher trait anxiety, state anxiety (before and after the cognitive tests) and higher debilitating anxiety scores. The migraine subjects

also demonstrated significantly higher levels of depression and lower vigor scores on the Profile of Mood States (POMS; McNair, Lorr & Droppleman, 1981). The authors statistically determined that those subjects with high depression, debilitating anxiety, high trait and state anxiety with low vigor scores did not perform as well on the cognitive tests; statistical correction did not render significant group differences in cognitive performance. Leijdekkers et al., (1990) attributed their contradictory findings to a number of variables. Firstly, they suggested their findings may have reflected a difference in subjects. Zeitlin and Oddy (1984) and Hooker and Raskin (1986) used migraine subjects who were participants in a migraine clinic and outpatients of hospitals. Leijdekkers et al.'s (1990) subjects had only rarely sought medical attention for their complaints. It is plausible these subjects suffered fewer side-effects and/or neurologic complications. Secondly, the Leijdekkers et al. (1990) study used a neuropsychologic battery containing relatively basic behavioural tasks as opposed to the more complex cognitive tests used in the other two studies. It was thought that this selection of tests

would remove the influences of education and baseline intelligence, something more complex tests could not control. As well, the Leijdekkers et al. (1990) battery required only 1 - 1 1/2 hours to complete compared to the longer administration times required for the other batteries. The authors noted that test sessions lasting longer than two hours may be measuring resistance to fatigue instead of cognitive abilities. Thirdly, the authors addressed the measurement of personality variables. They acknowledged that Zeitlin and Oddy (1984) had used personality measures and found higher free-floating anxiety, obsessionality and somatic complaints in the migraine group but remarked that the scales used were designed for psychiatric patients and likely not valid for a normal population. The self-report measures used in the Leijdekkers et al. (1990) study were for use with a normal population. They noted that several correlations between cognitive results and self-report measures had been found in their study and these were in the expected direction. They argued that the performance of the migraine subjects would be underestimated if not corrected for anxiety and arousal, as these are detrimental to

performance, especially for complex tasks. Leijdekkers et al., (1990) noted that Hooker and Raskin (1986) found that performance of migraine patients was particularly impaired for highly complex tests. From the above evidence, Leijdekkers et al., (1990) suggested that the observed differences in cognitive performance were a reflection of emotional variables rather than cumulative neurological dysfunction. Their finding of no relationship between headache history and cognitive performance further weakens the argument of cumulative cognitive impairment.

Rationale and Objectives of the Present Study

The purpose of the present pilot study was to further investigate the results presented in the papers by Zeitlin and Oddy (1984), Hooker and Raskin (1986) and Leijdekkers et al., (1990). In the study by Leijdekkers et al., (1990) several issues were raised as possible explanations for their contradictory findings. This study has attempted to conduct a more comprehensive study which further examines the earlier significant findings. To address the issues raised by Leijdekkers et al. (1990) this study has: included in

the battery both behavioural and more complex cognitive tests; used a battery which does not exceed 2 hours of administration time; included measures of emotionality/personality suitable for a normal population; included measures of subjective pain and assessed if medical treatment has been sought for migraine headache pain.

The inclusion of both basic "behavioural" and more complex cognitive tests, personality variables, a pain measure and an examiner-administrated versus a computer-administrated test battery renders a number of possible explanations depending on the results:

1) The **subjects** used may be the crucial factor. Migraine subjects who are outpatients or at a migraine clinic may experience more side effects and/or neurologic complications than subjects who have not sought medical attention for their headaches. The subjects in this study will be recruited from the community, and on this basis alone, would not be predicted to perform significantly different than the controls on the cognitive tests.

   The **type of test used** (complex cognitive versus

basic behavioural) may be the crucial factor. This can be argued two ways, however. If migraine subjects perform significantly more poorly on only complex cognitive tasks, they may experience deficits only in higher cognitive functioning, or, basic behavioural tests may not be sensitive enough to detect neuropsychological deficits if the tasks are too simple. What one considers to be a basic behavioural test versus a more complex cognitive task may be a discrepancy as well. **Method of testing** (computer-battery versus examiner-administrated) may be more important than the type of test per se. Two tests in the more basic "behavioural" computer-battery (Digit Symbol, Finger-Tapping) found to be nonsignificant in the study by Leijdekkers et al. (1990) were found to be performed significantly poorer by migraine subjects in the study by Hooker and Raskin (1986). If those tests found to be nonsignificant by Leijdekkers et al. (1990) and significant by Hooker and Raskin (1986) and Zeitlin and Oddy (1984) are again found significant using a community-based migraine

sample tested by an examiner, it would lend support to the hypothesis of method of testing being the important variable.

Personality variables may be responsible for differences in test performance. When the effects of personality variables are removed, it may be found that any differences in cognitive performance are removed, in the migraine sample.

5) **Fatigue** may be responsible for the differences in test performance. Leijdekkers et al. (1990) used a battery which was 1 1/2 hours in length, whereas, Hooker and Raskin (1986) used a battery requiring 2 - 3 hours for administration. No administration time was given in the study by Zeitlin and Oddy (1984).

If migraine subjects demonstrate significant differences in performance on cognitive tests, it is unclear if there will be differences between migraine with aura and migraine without aura subjects, as contradictory results were found in the studies by Hooker and Raskin (1986) and Leijdekkers et al. (1990).

There may be an interaction of pain, personality

variables, nature of the test, and method of administration with test performance, which will have to be analyzed further to determine if permanent cognitive deficits in migraine subjects is a reasonable hypothesis.

Method

Subjects

Subjects for the present study were recruited through newspaper, radio and television advertising in Thunder Bay and Toronto, Ontario, Canada. All of the migraine subjects fulfilled the criteria for migraine with aura and migraine without aura according to the criteria for the International Headache Society (1988) (see Appendix E). Only those subjects reporting a minimum of two migraine headache days per month for at least the previous two years were included. Migraine subjects taking daily preventative medication were also excluded from the sample. All migraine and control subjects also fulfilled the minimum inclusion/exclusion criteria (the majority taken from Leijdekkers et al., 1990; see Appendix D).

A total of 41 volunteers participated in the

study. Fourteen subjects were classified as migraine with aura (11 females, 4 males), fifteen classified as migraine without aura (10 females, 5 males) and twelve control subjects (9 females, 3 males).

One-way analysis of variance revealed no significant differences between groups with respect to age, $F < 1$, level of education, Chi-square (6) = 9.66, $p > .05$, or estimated IQ level (based on the WAIS-R Vocabulary subtest performance), $F < 1$. The mean group ages, distribution of education levels and mean group estimated IQ levels are presented in Table 1.

Materials

To determine if subjects initially met the inclusion/exclusion criteria, they were screened using a questionnaire. This was done in person or over the phone, at their convenience. The questionnaire is an adaptation of the Waters' Headache Questionnaire (1974), the classification and diagnostic criteria of the Headache Classification Committee of the International Headache Society (1988) and the inclusion/exclusion criteria from the study by Leijdekkers et al. (1990). It was used to collect the

Table 1

Mean Age and Range, Education Level and Mean Estimated IQ Level by Group

	Migraine with aura (n = 14)	Migraine without aura (n = 15)	Control (n = 12)
Age (years)	33.8	37.3	30.8
Range	22-49	19-49	21-46
Education Level*			
	0		0
	4		1
	0	0	0
	5	2	3
	5	8	8
Estimated IQ (Age-scaled)	12.7	11.9	12.6

*Education Level: 1 - High School Incomplete
2 - Grade 12 3 - Grade 13
4 - College 5 - University

following information: name, age, sex, occupation, education, medical history, medical attention sought (yes/no) and medication use related to their headaches (yes/no) as well as any other medication being used, handedness and headache history. The headache parameters were measured as follows: Headache History - the reported number of years since the subject experienced their first migraine headache attack; Headache Frequency - the reported average number of headaches per month; Headache Duration - the reported average number of hours a headache attack lasts; and Headache Intensity - the self-report rating using a severity index from 1 - 5:

1 - "I only have a headache if I pay attention to it"
2 - "I have a headache but it does not interfere with my work"
3- "I have a headache, and I have difficulty concentrating"
4 - "I have a headache and am unable to perform usual work, but bedrest is unnecessary"
5 - "I have a headache and bedrest is necessary"

(NOTE: Ideally, a headache diary of at least two weeks duration should have been used to obtain a more objective measure of headache history. However, due to the time restrictions, self-report measures were used).

The test battery was constructed using 5 of 10 tests identical to those for which performance was found to be significantly poorer in migraine subjects (Zeitlin & Oddy, 1984; Hooker & Raskin, 1986), and an additional 5 tests similar to those used in the relevant studies and/or shown to be highly sensitive to minimal brain dysfunction. The tests were as follows:

1) FINGER-TAPPING TEST (HRNTB, 1979): This is a measure of simple motor speed. Subjects must tap as rapidly as possible with the index finger on a small lever which is attached to a mechanical counter. They are given five 10-second trials with the dominant hand and then five trials with the nondominant hand. The procedure requires five consecutive trials that are within a 5-point range from fastest to slowest; a maximum of 10 trials per hand are administrated to achieve this criterion. The scores on this test are the average number of taps for five consecutive valid trials for the dominant hand and for five consecutive valid trials for the nondominant hand. This test was used in the studies by Hooker and Raskin (1986) and Leijdekkers et al. (1990); it

was significant only in the former study.

PACED AUDITORY SERIAL ADDITION TEST (PASAT; Gronwall & Wrightson, 1974): This test measures rate of information processing. Subjects are presented four random series of digits, at four standard rates of presentation (1-2 to 2-4 seconds interval). They are required to add each digit to the one preceding it and then give their answer (ie., the second digit is added to the first, the third to the second, etc.). Scores are expressed as the mean correct responses per second. This test was significant in the study by Zeitlin and Oddy (1984).

TRAILMAKING A, B (HRNTB, 1979): This test measures appreciation of symbolic significance of numbers and letters, scanning ability, flexibility and speed. In Part A, subjects must draw a line joining the numbers 1-25 in their correct numerical sequence. Part B requires subjects to systematically alternate between letters and numbers. Time to complete each form is measured. This test is one of the more sensitive general indicators of brain damage. This test was used in

the studies by Zeitlin and Oddy (1984) and Hooker and Raskin (1986). Trailmaking A was significant only in the former study.

4) ASSOCIATE LEARNING (Immediate and Delayed; Wechsler Memory Scale-Revised, 1987): This test measures verbal memory. Subjects are given six trials to learn eight word pairs. They are read the list of pairs and then read the first word of each pair and asked to recall the second word from memory. Four word-pairs reflect easy associations and four are more difficult. Scores reflect the number of correct associations for the first three trials only. After a 30-minute delay, subjects are again read the first word of each pair and asked to recall the second word from memory. This manually-administered associate learning test will be substituted for the computer-administrated version of the associate learning test used in the study by Leijdekkers et al. (1990) which did not yield a significant result.

5) DIGIT SYMBOL (Wechsler Adult Intelligence Scale-Revised, 1981): This test measures sustained attention, motor and psychomotor speed and visual-

motor coordination. Subjects must substitute symbols on a test form corresponding to their related numbers. This task is scored according to the number of correct substitutions completed during a 90-second interval. This test was used in the studies by Hooker and Raskin (1986) and Leijdekkers et al. (1990); it was significant only in the former study. Digit Symbol has consistently been found to be one of the most sensitive tests for brain damage, irrespective of localization (Guilandas et al., 1984, p.69).

6) LOGICAL MEMORY (Immediate and Delayed; Wechsler Memory Scale-Revised, 1987): This test is a measure of auditory perception, verbal comprehension and short and long-term memory. Subjects are read two stories and are asked to recall each verbatim. A subject's score is the sum of the total number of words remembered for each story. Following a 30-minute delay interval, subjects are again asked to recall each story verbatim and a delayed recall score is calculated. This test was significant in the study by Hooker and Raskin (1986) and is considered one of the

tests most sensitive to brain damage (Guilandas et al., 1984, p.69).

BUSCHKE SELECTIVE REMINDING TEST (Buschke, 1973): This test is a measure of verbal learning and memory. Subjects are read a list of 12 unrelated words at a rate of one word every two seconds. The subject is asked to recall the list, in any order. Following this, subjects are selectively reminded only of those words that they did not recall in the previous trial and are again asked to recall the list, in any order. This continues for five trials. Subjects receive a score reflecting the number of items learned (LTS - long-term storage) and a score reflecting consistent long-term retrieval (cLTR). This test was not included in the previous batteries but has been found to be clinically useful for analyzing impaired memory (Buschke & Fuld, 1974).

8) CONTROLLED WORD ASSOCIATION TEST (HRNTB, 1979): This test is a measure of expressive language and speech. It involves a symbolic factor rather than being purely semantic, as word meaning is irrelevant when retrieval is from different

logical categories. Subjects are asked to name as many words as they can beginning with the letters F, A and S during three 60-second trials. Scoring is based on the number of correct words generated. This test was not used in the earlier studies but is considered to be sensitive to cognitive deficits.

9) VISUAL SEARCH AND ATTENTION TEST (Trenerry, Crosson, DeBoe & Leber, 1990): This visual-motor test provides measures of sustained attention and visual scanning. Subjects are given a number of visual cancellation tasks which vary in complexity and familiarity. A total score and a left and right score are calculated. This test was not used in the previous studies but was selected to substitute for the computer-administrated sustained attention test in the study by Leijdekkers et al. (1990) which was not significant. Attention and concentration are commonly impaired in individuals with brain damage (Lezak, 1983; as cited in Trenerry et al., 1990).

10) VOCABULARY (Wechsler Adult Intelligence Scale-Revised, 1981): This test is a measure of general

knowledge and will be used as an estimate of intellectual ability. Performance on this test has been shown to be stable over time and relatively resistant to neurological deficit and psychological disturbance (Blatt & Allison, 1968; as cited in Sattler, 1990, p.151). The test consists of 35 words in order of increasing difficulty. Subjects are presented with each word orally and in writing and are asked to give the definitions of each word. Each response is scored 0-2 according to level of accuracy and the test is discontinued after five consecutive failures.

The five original tests found to be significant in the previous studies (Trailmaking A, Finger-Tapping, Logical Memory, Digit Symbol and the PASAT) were included for cross-validation.

The Visual Search and Attention Test and Verbal Associate Learning (similar to tests in the NES) were included in the battery even though they were not significant in the study by Leijdekkers et al. (1990). Digit Symbol and Finger-Tapping were also not significant in that study but were significant in the

study by Hooker and Raskin (1986). This discrepancy could be attributed to using a computer battery or to the differences in migraine severity of subjects between these studies, suggested by Leijdekkers et al. (1990). Therefore, all four tests were included to examine these hypotheses. As well, these four tests were operationally defined as the "behavioural" tests of the battery, as Leijdekkers et al. (1990) suggested the tests in their battery were relatively basic behavioural tests rather than complex cognitive tasks which are too linked to background variables such as education and baseline intelligence.

The Controlled Word Association Test was included to assess expressive language, one of the significant complaints of migraine patients in the study by Hooker and Raskin (1986).

The Buschke Selective Reminding Test has been included to assess both verbal learning and memory and semantic organization. It allows for a comparison of item-learning versus list-learning ability, and has been demonstrated to be clinically useful for analyzing impaired memory (Buschke & Fuld, 1974).

All subjects were administered six questionnaires

assessing personality variables. The three measures found to yield significant differences among migraine and nonheadache subjects were included. The questionnaires were as follows:

1) PROFILE OF MOOD STATES (POMS; McNair, Lorr & Droppleman, 1981): This 65-item self-report questionnaire yields scores on 6 factor-analytically derived scales of fatigue, depression, anger, tension, confusion-bewilderment and vigor. Subjects are asked to rate on a 5-point Likert scale how they have been feeling during the past week including today. This measure was used in the study by Leijdekkers et al. (1990).

   STATE-TRAIT ANXIETY INVENTORY (STAI; Spielberger, 1983): Two 20-item self-report questionnaires assess "state" anxiety (an emotional reaction which varies from one situation to another) and "trait" anxiety (a personality characteristic, it is characteristic of the person and not the situation). This measure was used in the study by Leijdekkers et al. (1990).

   ASSESSMENT OF OWN FUNCTIONING INVENTORY (Chelune,

Heaton & Lehman, 1986): This 34-item self-report questionnaire was designed to elicit patients' self-perceptions regarding the adequacy of their functioning in various everyday tasks and activities. The 5 factor-analytically derived scales are memory, language and communication, use of hands, sensory-perceptual and higher level cognitive and intellectual functions. Subjects are asked to answer on the basis of current functioning between migraine attacks. This measure was used in the study by Hooker and Raskin (1986).

The Profile of Mood States and the State-Trait Anxiety Inventory indicated significant differences in a number of personality variables in the study by Leijdekkers et al. (1990). These measures are appropriate for use with normal populations. Use of the Assessment of Own Functioning Inventory was criticized by Leijdekkers et al. (1990) because it was designed for psychiatric populations, but it was also included in the current study for cross-validation of previous findings as it also indicated significant

differences in the study by Hooker and Raskin (1986).

4) BECK DEPRESSION INVENTORY (BDI; Beck & Beck, 1972): This 21-item self-report questionnaire provides a quantitative assessment of the depth or intensity of depression. The BDI was included as an additional measure of depression, one of the symptoms found to be significantly different in migraine subjects versus controls. This measure is suitable for use with a normal population.

5) VISUAL ANALOGUE PAIN RATING SCALE (Huskisson, 1974; as cited in McDowell & Newell, 1987): This is a simple method of recording subjective estimates of pain intensity. Subjects are presented with a horizontal line, 100mm in length. At each end of the line are labels indicating the range of pain from "no pain" to "unbearable pain". "Severe", "moderate" and "slight" ranges are indicated along the line. Subjects are requested to place a mark on the line representing the severity of their pain. The distance, in millimetres, from the end labelled "no pain" is recorded. The Visual Analogue Pain Rating Scale was included to provide some measure of subjective

pain to assess for individual differences. This measure is suitable for use with a normal population.

6) HEALTH LOCUS OF CONTROL (HLC) SCALE (Wallston, Wallston, Kaplan & Maides, 1976): This 11-item self-report questionnaire is an area-specific measure which has attempted to operationalize health-related locus of control beliefs. Subjects are classified as "internal" or "external" with respect to their belief of locus of control. Lower scores are associated with an internal locus. Internals are more likely than externals to take steps to better their environmental condition, according to Social Learning theory (Rotter, Chance & Phares, 1972; as cited in Wallston et al. 1976). This measure has been included to help discriminate those subjects who might become more anxious during testing, because of their locus of control. This is important because anxiety may impair test performance. This questionnaire was not used in previous studies.

In addition, a pre-testing Session and post-

testing Session Follow-Up self-report questionnaire was administrated:

7) SESSION QUESTIONNAIRE: Subjects were asked the following questions before the testing session began:

   a) Have you taken any medication in the last 24 hours? (medication name, dosage and time taken were recorded).

   b) Have you had any alcohol in the last 24 hours? (If a subject answered 'yes', the session was terminated).

   c) Do you presently have a headache? (If a subject answered 'yes', the session was terminated).

   d) Where are you in your menstrual cycle? (female migraine subjects only). This question was included to provide a possible covariate should performance be found to be impaired in the migraine subjects.

8) SESSION FOLLOW-UP CHECKLIST: Subjects were asked the following questions after the test session was completed:

   a) Were you worried about getting a headache

during the session?

b) Did you develop a headache during the test session?

:) Were you feeling fatigued during the testing? If YES, when? Can you rate it from 1-10? (1 being not tired).

Procedure

Subjects were selected based on the information obtained in the initial interview/questionnaire. A mutually convenient appointment was arranged to administer the test battery. The test sessions were conducted individually, by the principle investigator.

The testing session proceeded in the following manner. The Session Questionnaire was first completed to determine if the test session could proceed. Subjects were first asked to fill out the State Anxiety form of the STAI. The battery was then administered in the following order: Finger Tapping Test, PASAT, Trailmaking A and B, Associate Learning (Immediate), Digit Symbol, Logical Memory (Immediate), Buschke Selective Reminding Test, Controlled Word Association Task, Visual Search and Attention Test, Vocabulary,

Associate Learning (Delayed) and Logical Memory (Delayed). Subjects were again asked to complete the State-Anxiety form of the STAI.

Subjects were then asked to fill out a number of questionnaires to assess common characteristics in migraine subjects. The questionnaires were given in this order: Profile of Mood States, the Trait Anxiety form of the STAI, Assessment of Own Functioning questionnaire, Beck Depression Inventory, the Visual Analogue Pain Rating Scale, the Health Locus of Control Scale. The Session Follow-up Checklist was administered following the entire battery.

Following completion of the test session, subjects were told that the study results would be available to them following completion of the project. Any interested subjects will be mailed the results.

Data Analysis

To check for group differences prior to testing, migraine with aura, migraine without aura and the control subjects were compared for any differences in age, level of education and estimated IQ using analysis of variance.

The migraine groups were compared on reported headache history, frequency, intensity and duration using independent t-tests. In addition, two severity indices were computed. Severity Index I was derived by rank ordering headache duration, frequency and history separately. These ranks were summed for each subject and then rank ordered. Severity Index II was an estimate of the total number of headache hours suffered by each subject (average duration X frequency X history); these estimates were then rank ordered (as used in the study by Zeitlin & Oddy, 1984). Independent t-test comparing migraine classifications on the Severity Indices were computed. A Spearman correlation of the two severity indices was also computed.

Group differences in headache intensity (severity rating from 1 - 5) and typical headache pain (as measured by the visual analogue scale) were compared using an analysis of variance.

Group differences on the personality measures of aged-scaled state anxiety (pre- and post-testing) and trait anxiety scores, raw depression scores, raw Health Locus of Control scores, and raw Assessment of Own

Functioning total scores were compared using analysis of variance. In addition, two discriminant analyses were used to determine if there were any group differences on the subscales of the Assessment of Own Functioning questionnaire and the Profile of Mood Scales (POMS).

Scores for each cognitive test, including trials of immediate/delayed where applicable, were calculated for each subject.

An impairment index was calculated for each subject to reflect the number of tests for which the score was greater than one or two standard deviations worse than the average score for the whole group. A value of one or two was assigned to scores below one or two standard deviations, respectively, and summed for each subject. This index was used in the study by Leijdekkers et al. (1990).

The scores for the cognitive tests were clustered and analyzed using four separate multivariate analyses of variance comparing group performance (migraine with aura, migraine without aura, controls). These clusters were taken from the Leijdekkers et al. (1990) study; the present study tests which differed from the

original study were placed in the cluster deemed most appropriate. The four clusters were as follows: "Reaction Time" (VSAT (right, left, total), PASAT (trials 1-4)); "Motor Speed" (Fingertapping (dominant and nondominant hand); "Psychomotor Ability" (Digit Symbol, Trailmaking A,B); "Learning and Memory" (Associate Learning (immediate, delayed), Logical Memory (immediate, delayed), Buschke Selective Reminding Test (cLTR, LTS), and the Controlled Word Association Test (F,A,S)).

One-way analyses of covariance comparing groups, using age as a covariate, were also conducted for those cognitive tests which did not have age-scaled scores, to check for any differences not captured by the raw scores alone. The cognitive tests assessed included: Fingertapping, PASAT, Trailmaking, Buschke Selective Reminding Test and the Controlled Word Association Test.

To compare group performance on those cognitive tests considered "basic behavioural" versus "complex cognitive", the nine tests were placed into one of the two categories. Within each category, the test scores for all subjects were factor analyzed to obtain a

factor loading for each test (and/or subtests). A "cognitive" and a "behavioural" score was computed for each subject by multiplying each individual's scores by the appropriate test factor loading and summing the products. A multivariate analysis of variance was then conducted comparing the three groups.

The same procedure, as above, was followed to compute a "right" and a "left" hemisphere score for each subject, based on those tests thought to require more "right" or "left" hemisphere processing. A multivariate analysis of variance was conducted using both group and "usual headache side" as independent variables. "Usual headache side" was included to determine if this variable had any influence on performance.

Pearson Product-Moment Correlation Coefficients were computed to determine if Headache History, education level, trait or state anxiety levels, and/or the two Severity Indices were significantly related to performance on any of the cognitive tests.

One-way analyses of variance were computed to determine if there were any significant differences in performance for those subjects indicating they

experienced some fatigue during testing versus those subjects who did not indicate feeling fatigued.

An intercorrelation matrix of all cognitive tests was computed to assess for internal consistency of performance on the cognitive tests.

Frequencies by group were computed for the responses given to the questions found in the Session, Session Follow-Up and Initial Screening questionnaires.

Post-hoc analyses were conducted to further analyze any significant main effects or interactions.

Results

The comparison of reported headache parameters between the migraine with aura and migraine without aura subjects yielded no significant differences between groups for Headache History (number of years), Intensity (severity rating from 1-5 (see Appendix C)) or Duration (average length of headache (hours)), $F < 1$. However, the migraine without aura subjects reported a significantly higher Headache Frequency (average number of headaches per month) than the migraine with aura subjects, t (27) = -2.23, p = .034. A Pearson correlation of headache frequency and

cognitive performance did not reveal any significant relationships between performance and frequency. There was no significant difference between the migraine groups on both Severity Index I, t (27) = -1.21, $p > .05$, and Severity Index II, t (27) = -0.45, $p > .05$. In addition, Severity Index I and II were found to be highly correlated (Spearman $r = .7150$, $p < .001$). The group means for the headache parameters are presented in Table 2.

The majority of the control subjects reported having non-migraine type headaches about once per year to several times per year (only two subjects reported having headaches about once per month), and no control subject indicated an average Intensity rating greater than "2" (mean = 1.8, sd = .45).

The comparison of reported Headache Intensity X Group yielded a significant difference between groups, F (2,38) = 27.18, $p < .001$. Post-hoc analyses revealed that both migraine with aura (mean = 4.1, sd = 1.1) and migraine without aura subjects (mean = 4.1, sd = 1.0) reported significantly higher headache intensity ratings ("I have a headache and am unable to perform usual work, but bedrest is unnecessary") than did the

Table 2

Mean Headache History, Frequency, Intensity and Duration by Headache Classification

	Migraine with aura Mean (sd)	Migraine without aura Mean (sd)
History (years)	16.9 (9.5)	16.8 (8.9)
Frequency (avg/mo.)	3.6 (1.6)*	6.8 (5.0)*
Intensity (severity rating)	4.1 (1.1)	4.1 (1.0)
Duration (hours)	32.7 (26.9)	31.1 (27.0)

*p < .05. **p < .01.

control subjects (mean = 1.8, sd = .45) ("I have a headache but it does not interfere with my work"). This finding was consistent with the comparison of Typical Headache Pain (as rated on a visual analogue from "no pain" to "unbearable pain") X Group, F (2,38) = 58.64, $p < .001$. Post-hoc analyses again revealed that migraine with aura (mean = 81.4, sd = 14.3) and migraine without aura subjects (mean = 80.1, sd = 11.6) indicated experiencing significantly higher levels of headache pain (severe to unbearable range) than did the control subjects (mean = 25.4, sd = 18.8) (slight to moderate range).

The comparison of State-Anxiety Pre-Testing X Group yielded no significant main effect of group, $F < 1$. The comparison of State Anxiety Post-Testing X Group did yield a significant main effect of group, F (2,38) = 4.23, $p = .022$. Post-hoc analyses revealed that the migraine with aura subjects (mean 67.4, sd = 27.4) reported significantly higher state anxiety scores after the test session than the control group (mean = 36.2, sd = 32.8). Although all of the comparisons were not significant, it was observed that group mean state anxiety levels were consistently

higher for the migraine subjects than the control subjects both at pre (mean = 49.5, 37.4, 29.3) and post-testing (mean = 67.4, 52.4, 36.2) (migraine with aura, migraine without aura and control subjects, respectively) and that state anxiety increased over the testing session consistently across groups.

The comparison of Trait Anxiety X Group yielded a significant difference between groups, F (2,38) = 4.79, p = .014. Post-hoc analyses revealed that trait anxiety scores for the migraine with aura (mean = 70.8, sd = 22.0) and migraine without aura subjects (mean = 63.1, sd = 29.7) were significantly higher than for the control group (mean = 38.5, sd = 30.2).

The comparison of Depression scores X Group did not yield a significant main effect of group, $F < 1$. It should be noted that the average depression score for the migraine subjects (mean = 8.6, sd = 6.7) was higher than for the control subjects (mean = 4.0), sd = 5.2), however, both means fell within the normal range.

The comparison of Health Locus of Control X Group did not yield a significant main effect of group, $F <$ 1. The average score for all three groups fell into the middle of the possible score range, indicating

subjects fell on average midway between an internal and external locus of control.

The comparison of Assessment of Own Functioning score X Group did not yield a significant main effect of group, $F < 1$. The mean total score for the migraine with aura subjects (mean = 38.6, sd = 17.4) was higher than the migraine without aura subjects (mean = 29.9, sd = 12.6) whose scores were also higher than the control group (mean = 26.9, sd = 14.6). The discriminant analysis comparing each subscale of the questionnaire X Group produced two discriminant functions, neither of which were significant (Chi-Square (10) = 11.80, Chi-Square (4) = 2.25, $p > .05$). Therefore, there were no significant differences between groups on those items assessing memory, language communication, use of hands, perceptual abilities and cognitive-intellectual abilities.

The discriminant analysis comparing the subscales of the POMS X Group also produced two discriminant functions, neither of which were significant (Chi-Square (12) = 13.62, Chi-Square (5) = 5.54, $p > .05$). Therefore, there were no significant differences between groups on ratings of depression, anger,

tension, vigor, confusion-bewilderment and fatigue.

The mean personality scores by group are presented in Table 3.

The comparison of the Impairment Index X Group yielded no significant main effect of group, $F < 1$. There was no significant difference between groups on the number of cognitive tests which were performed at a level of one or two standard deviations below the mean of the entire sample.

The multivariate analysis of the Reaction Time cluster X Group yielded no significant main effect of group, $F < 1$. In addition, none of the individual univariate F-tests were significant at the .05 level. Therefore, there were no significant differences in performance between groups on the Visual Search and Attention Test (right, left or total score) or the Paced Auditory Serial Addition Test (all rates of presentation).

The multivariate analysis of the Motor Speed cluster X Group yielded no significant main effect of group, $F < 1$. No significant univariate tests were found to be significant. Therefore, there was no significant difference in performance between groups on

Table 3

Mean Personality Scores by Group

	Migraine with aura Mean (sd)	Migraine without aura Mean (sd)	Control Mean (sd)
State Anxiety			
Pre	49.5 (20.3)	37.4 (21.9)	29.3 (28.7)
Post	67.4 (27.4)*	52.4 (22.0)	36.2 (32.8)*
Trait Anxiety	70.8 (22.0)*	63.1 (29.7)*	38.5 (30.2)*
Depression	8.8 (6.0)	8.4 (7.5)	4.0 (5.2)
Health Locus	31.9 (6.5)	33.9 (9.4)	27.9 (6.7)
Assessment of Own Functioning			
Total Score	38.6 (17.4)	29.9 (12.6)	26.9 (14.6)
Memory	13.8 (8.2)	10.2 (6.3)	12.4 (6.7)
Language	12.3 (8.2)	8.8 (4.7)	6.8 (4.4)
Use of Hands	2.6 (2.2)	2.2 (1.5)	1.9 (1.4)
Perceptual	1.6 (1.5)	1.6 (2.0)	0.9 (1.8)
Intellectual	8.3 (4.1)	7.1 (4.6)	4.8 (3.9)

Table 3 - continued

Mean Personality Scores by Group

	Migraine with aura Mean (sd)	Migraine without aura Mean (sd)	Control Mean (sd)
Profile of Mood States			
Depression	9.3 (6.7)	9.9 (9.5)	7.8 (11.5)
Anger	10.3 (7.5)	6.5 (6.6)	7.1 (6.3)
Fatigue	10.7 (5.0)	10.5 (6.5)	6.3 (5.1)
Vigor	16.0 (5.4)	19.0 (7.1)	20.3 (5.6)
Tension	12.1 (5.4)	11.1 (5.8)	8.5 (6.0)
Confusion	7.9 (4.4)	7.5 (3.2)	5.8 (6.3)

*p < .05. **p < .01.

the Fingertapping test (dominant or nondominant hand).

The multivariate analysis of the Psychomotor Ability cluster X Group did not yield a significant main effect of group, $F < 1$. No significant univariate tests were revealed. Therefore, there was no significant difference in performance between groups on the Digit Symbol test or the Trailmaking Test (A, B).

The multivariate analysis of the Learning and Memory cluster X Group did not yield a significant main effect of group, $F < 1$. There were however, two cognitive tests which were significantly different between groups based on the univariate comparisons: Associate Learning - immediate recall, F (2,37) = 4.66, p = .016, and the Controlled Word Association Test - trial S, F (2,37) = 4.3, p = .021. Although the overall multivariate test was not significant, post-hoc analyses were conducted to determine if these differences revealed poorer performance in the hypothesized direction. Post-hoc analyses for the Associate Learning test - immediate recall, revealed that the migraine with aura subjects (mean = 21.9, sd = 2.1) recalled significantly more word pairs than did the migraine without aura subjects (mean = 18.4, sd =

4.1). Post-hoc analyses of the Controlled Word Association test - trial S, revealed that the migraine with aura subjects produced significantly more words during the trial (mean = 19.0, sd = 4.2) than did both the migraine without aura subjects (mean = 14.8, sd = 4.3) and the control subjects (mean = 15.5, sd = 3.8). These group differences, therefore, do not provide evidence to support the main hypothesis.

To determine if there were any differences in cognitive performance due to medication use for migraine relief, or due to medication use 24 hours prior to testing, two multivariate analyses were re-run for each of the four cognitive test clusters. None of the multivariate comparisons were found to be significant for the main effects of medication use or medication taken 24 hours prior to testing, $F < 1$. However, the univariate comparisons of medication taken 24 priors to testing were significant for the Digit Symbol test, F (1,28) = 8.60, p = .007, and the Visual Search and Attention Test (left, right and total scores), F (1,34) = 5.89, p = .021, F (1,34) = 7.88, p = .008 and F (1,34) = 7.15, p = .011, respectively. To further assess these findings, raw scores for the seven

subjects who had taken medication 24 hours prior to testing (1 migraine with aura, 5 migraine without aura, 1 control) were compared to the sample means for each test. The mean scores of the seven subjects were found to be higher than the mean of the entire sample for the Visual Search and Attention Test (left, right, total) and the Digit Symbol test. Individually, only two subjects from the seven (migraine without aura group) had raw scores below the sample mean for the VSAT (left, right and total) and only one subject of the seven (migraine without aura group) had a raw score below the sample mean for the Digit Symbol test. These analyses, therefore, suggest that medication use 24 hours prior to testing did not have an overall negative effect on cognitive performance. The analyses comparing cognitive performance and medication use should be accepted with some caution, as only three of the twenty-nine migraine subjects reported not using medication regularly to relieve migraine headache pain. However, because there were no significant differences between groups in the hypothesized direction, it does not appear that medication use had a negative influence on performance.

The multivariate analyses of the cognitive clusters were also re-run using trait and state-anxiety (pre- and post-testing) as covariates. No significant differences between groups were observed over those noted in the original cluster analyses, $F < 1$. Therefore, anxiety did not appear to have a significant negative effect on performance.

When the effects of age were covaried out, the comparisons of Fingertapping scores (dominant, nondominant hand) and PASAT scores (all presentation rates) X Group did not reveal a significant main effect of group, $F < 1$.

The comparison of Trailmaking scores (A,B) X Group using age as a covariate yielded no significant main effect of group but revealed that age explained a marginally significant amount of the variance in performance scores for Trailmaking B, F (1,36) = 3.81, $p = .060$. A Pearson correlation coefficient was computed to determine the direction and magnitude of the relationship between age and Trailmaking B scores, yielding a coefficient of $r = .3171$, n.s. Therefore, Trailmaking B speeds show some decrease with age, but this relationship was not significant. Age and

performance on the Trailmaking A test were not significantly related. In addition, as there was no main effect of group when the effect of age was also controlled, this finding does not support the main hypothesis.

The comparison of the Buschke Selective Reminding test scores (cLTR, LTS) X Group with age as a covariate revealed that age explained a significant proportion of the variance in performance scores for consistent long-term retrieval (cLTR), $F(1,37) = 6.03$, $p = .019$. A Pearson correlation coefficient was computed to assess the direction and magnitude of the relationship between age and cLTR, yielding $r = -.3648$, $p < .05$. Therefore, as age increases, subjects demonstrated a significant decrease in the ability to consistently recall words recalled previously over five trials. There was no significant relationship found between age and the number of words recalled on two successive trials (Long-Term Storage). As there was no main effect of group when the effect of age was also controlled, this finding does not support the main hypothesis.

The comparison of Controlled Word Association scores (trials F,A,S) X Group using age as a covariate

yielded no significant main effect of group or age, $F < 1$. Therefore, age was not significantly related to the number of words subjects generated during each trial.

The multivariate comparison of "Cognitive" tests versus "Behavioural" tests X Group yielded no significant main effect of group, $F < 1$. Neither of the univariate comparisons were found to be significant. Therefore, there were no significant differences between groups in their performance for either the "cognitive" or "behavioural" tests.

The multivariate comparison of "Left" and "Right" hemisphere tests X Group yielded no significant main effect of group, $F < 1$. Neither of the univariate comparisons revealed a significant group difference. Therefore, there were no significant differences in performance between groups on either the "left" or "right" hemisphere cognitive tests. A second multivariate analysis of "Left" and "Right" tests X Group (migraine only) X Usual Headache Side also yielded no significant main effects or an interaction, $F < 1$. Therefore, there appears also to be no significant relationship between cognitive performance differentiating general hemisphere processing and the

side of the head one usually experiences a migraine headache.

The mean cognitive performance score by test and group are presented in Table 4.

The Pearson correlations of Headache History with cognitive test scores (migraine subjects only) yielded only one significant correlation between headache history and consistent long-term retrieval (Buschke Selective Reminding test), $\underline{r} = -.3940$, $p < .05$. Therefore, as headache history increases, migraine subjects' ability to consistently recall words, recalled previously, over five trials significantly decreases. Headache history is also a function of age; this finding therefore probably reflects the age effects on memory rather than a direct relationship between headache history and memory.

The Pearson correlations of Education Level and cognitive test scores (all subjects) yielded a significant correlation of education level and dominant hand performance (Fingertapping), $\underline{r} = .3477$, $p < .05$, and education level with the PASAT (presentation speed 2.0 seconds), $\underline{r} = -.3941$, $p < .05$. Therefore, subjects with a higher education level produced significantly

Table 4

Mean Cognitive Performance Scores by Cluster and Group

Test	Migraine with aura Mean (sd)	Migraine without aura Mean (sd)	Control Mean (sd)
Impairment Index	2.6 (2.1)	5.3 (5.8)	3.3 (3.3)
Reaction Time			
VSAT (age-normed)			
Right	43.7 (30.8)	40.3 (29.5)	49.7 (23.0)
Left	45.3 (32.1)	42.7 (29.6)	49.8 (23.5)
Total	44.2 (31.7)	41.7 (29.9)	49.6 (22.7)
PASAT (time/correct response)			
2.4 sec	3.4 (0.9)	3.6 (0.9)	4.1 (1.3)
2.0 sec	3.1 (0.8)	3.3 (0.9)	3.1 (0.6)
1.6 sec	2.8 (0.7)	3.1 (0.8)	3.0 (0.9)
1.2 sec	3.4 (1.1)	4.0 (3.0)	4.2 (2.8)
Motor Speed			
Fingertapping (average/10 sec)			
Dominant	57.5 (6.1)	55.7 (6.0)	56.6 (7.1)
Nondominant	53.2 (4.9)	50.4 (5.5)	49.5 (5.2)

Table 4 - continued

Mean Cognitive Performance Scores by Cluster and Group

Test	Migraine with aura Mean (sd)	Migraine without aura Mean (sd)	Control Mean (sd)
Psychomotor Speed			
Digit Symbol (age-normed)	13.1 (2.3)	11.9 (2.2)	12.2 (1.5)
Trailmaking (total seconds)			
A	20.0 (6.9)	17.9 (3.6)	18.8 (7.6)
B	54.3 (15.8)	50.1 (15.3)	48.3 (16.5)
Learning and Memory			
Logical Memory (age-normed)			
Immediate	77.2 (27.6)	75.2 (25.1)	86.6 (11.3)
Delayed	78.4 (23.4)	66.0 (27.5)	82.9 (10.4)
Associate Learning (number correct)			
Immediate	21.9 (2.1)*	18.4 (4.1)*	19.8 (2.6)
Delayed	7.6 (0.6)	7.3 (0.8)	7.7 (0.7)
Selective Reminding (total for 5 trials)			
cLTR	8.7 (3.5)	6.8 (4.3)	9.7 (2.8)
LTS	11.1 (1.2)	9.5 (3.4)	11.0 (1.5)

Table 4 - continued

Mean Cognitive Performance Scores by Cluster and Group

Test	Migraine with aura Mean (sd)	Migraine without aura Mean (sd)	Control Mean (sd)
Learning and Memory - continued			
Controlled Word Association (total correct words)			
F	16.5 (4.2)	14.9 (4.0)	15.2 (4.0)
A	13.2 (3.2)	11.3 (4.2)	12.6 (3.2)
S	19.0 (4.2)*	14.8 (4.3)*	15.5 (3.8)*

*p < .05. **p < .01.

more taps per ten-second trial than subjects with a lower education level. In addition, as education level increases, the time per correct response decreases significantly at the presentation rate of 2.0 seconds per item. Education level alone cannot account for any differences in performance.

The Pearson correlations of Trait Anxiety and State Anxiety (pre and post) and cognitive test scores yielded only one significant correlation between state anxiety pre-testing and the Controlled Word Association test - trial A, $\underline{r} = -.3482$, $p < .05$. Overall, however, there does not appear to be a significant relationship between trait (-.3032 to .2079) or state anxiety (pre: -.3482 to .2276, post: -.2731 to .2040) and cognitive performance.

The Pearson correlations of Severity Index I and Severity Index II with the cognitive test scores did not yield any significant relationships. Therefore, there is no evidence to suggest that cognitive performance is related to headache severity, as estimated by both headache frequency, duration and history rank ordered and summed (Severity Index I, -.3239 to .2399) or an estimate of the total number of

headache hours suffered (Severity Index II, -.3041 to .3258).

The one-way analyses of variance comparing subjects who indicated they did (N = 11) versus did not (N = 30) experience some fatigue during testing versus performance revealed a significant difference between responding groups for the Controlled Word Association Test - trial S, F (1,39) = 10.00, p = .0030, and Trailmaking B, F (1,35) = 9.95, p = .0033. Subjects who indicated fatigue during testing (mean = 62.79, sd = 11.54) had significantly slower performances on the Trailmaking B test than subjects who did not (mean = 46.5, sd = 14.7). However, subjects indicating fatigue (mean = 19.73, sd = 3.9) also produced significantly more words than subjects who did not on the Controlled Word Association test - trial S (mean = 15.23, sd = 4.1). These results, therefore, suggest that if fatigue was experienced during testing, it did not have an overall significant negative effect on performance.

Frequency data by group on the Session and Session Follow-Up questionnaire are presented in Table 5.

Frequency data by group on the questions regarding headache characteristics in the Initial Screening

Table 5

Response Frequencies to Session and Session Follow-up Questionnaires by Group

Question	Migraine with aura (n = 14)	Migraine without aura (n = 15)	Control (n = 12)
Med Use 24H prior to testing? Yes			
Worried about developing a headache? Yes			
Developed a headache during testing? Yes			
Fatigued during testing? Yes			

Questionnaire are presented in Table 6.

As a final check, the cognitive performance of the sample was compared to available norms (based on control subjects) to rule out the possibility that our sample performed at an impaired level, particularly our control group, which would prevent finding any significant differences between migraine subjects and controls.

Normative data for the Fingertapping Test was obtained from two sources: Jarvis and Barth (1984, p. 22) and Russell, Neuringer and Goldstein (1970). Russell et al. (1970) collected revised norms for rating equivalents of raw scores for a number of neuropsychological tests using a rating scale from 0 (high normal) to 5 (severe impairment). A rating score of "2" designates the beginning of the impaired range. The dominant hand mean for the entire sample fell above the impaired range using both norms. However, seven subjects (2 migraine with aura, 3 migraine without aura, and 2 controls) fell into the impaired range based on the Jarvis and Barth (1984) norms, while three subjects (2 migraine with aura, 1 migraine without aura) fell into the impaired range (rating of 2) using

Table 6

Frequency Data of Migraine Characteristics by Group

	Migraine with aura (n = 14)	Migraine without aura (n = 15)	Control (n = 12)
Gender			
Male			
Female		10	
Sought Rx from Neurologist		4	
Unilateral Headache			
Never			
Sometimes			
Usually			
Always			
Usual Headache Side			
Right			
Left			
Mixed			
Left or Right			
Known Triggers? Yes	13	12	

Table 6 - continued

Frequency Data for Migraine Characteristics by Group

	Migraine with aura (n = 14)	Migraine without aura (n = 15)	Control (n = 12)
Usual Headache Symptoms (Yes)			
Changes in Sight	13		
Changes in Appetite	14	12	
Dizziness	10	13	
Sleepiness	6	6	
Ringing in Ears	5	6	
Sensitivity to Noise	13	11	
Sensitivity to Light	14	12	
Tingling in Body	9	4	
Aggravated by performing routine activities			
Nausea/Vomiting			
usually feel sick			
usually vomit		˘	˘

Table 6 - continued

Frequency Data for Migraine Characteristics by Group

	Migraine with aura (n = 14)	Migraine without aura (n = 15)	Control (n = 12)
Hours or a day before a headache, do you experience:			
Hypoactivity			
Hyperactivity			
Depression			
Crave Certain Foods			
Repetitive Yawning			
Menstruation a Trigger			
Do you use medication to treat migraine pain? (yes)	12	14	N/A

the Russell et al. (1970) norms for the dominant hand. One migraine without aura subjects also fell into the impaired range for the nondominant hand trial using the Russell et al. (1970) norms.

Normative data for the Paced Auditory Serial Addition Test from Gronwall and Wrightson (1974; in Lezak, 1976) was used. The entire sample mean at each presentation rate fell below the performance of the control normative sample. On examination of the individual scores, it was observed that approximately 57% of the migraine with aura, 73% of the migraine without aura and 71% of the control subjects fell below the normative score at each presentation rate. However, because the standard deviations were not included, the relative performance of this sample could not be more precisely compared.

Normative data for the Trailmaking test was also obtained from two sources: Jarvis and Barth (1984) and Russell et al. (1970). The entire sample means were found to fall within the non-impaired range for both form A and B, using both norms. No individual subjects fell into the impaired range using the Jarvis and Barth (1984) norms, whereas, two subjects (1 migraine with

aura, 1 control) achieved a rating of "2" using the Russell et al. (1970) norms.

Normative data for the Digit Symbol test was obtained from Russell et al. (1970). The entire sample mean fell above the impaired range. One migraine without aura subject achieved a rating of "2" on the impaired scale.

Normative data for the Visual Search and Attention test was obtained from the test manual (Trenerry, Crosson, DeBoe and Leber, 1990). Scores below the 16th percentile were noted as being indicative of brain damage. The entire sample means were found to be in the normal range for the right, left and total scores. However, an assessment of the individual scores indicated that seven subjects (2 migraine with aura, 4 migraine without aura, 1 control) had scores below the 16th percentile for the right, left and total scores. One additional migraine without aura subject had a score in the impaired range for the right total.

Normative data for the Associate Learning Test was found in Lezak (1976). No impairment cut-off scores were provided but performance relative to the summed score of the age 30-39 standardization sample was

examined. The entire sample mean for the immediate trial was higher than the mean of the standardization group. One migraine without aura subject had a summed score below one standard deviation of the standardized norms. No norms were available for the delayed trial performance, however, the three groups (migraine with aura, migraine without aura, control) recalled an average of 7.6, 7.3, and 7.7 words out of 8 =, respectively.

Only the norms for the standardization sample between two age ranges were available for the Logical Memory test (Lezak, 1976). Therefore, since age-scaled percentile ranks were used in assembling the present data, scores below the 25th percentile were considered below average. The entire sample mean for both the immediate and delayed trials were above average. One migraine with aura subject had scores falling below the 25th percentile at both testings. Two subjects (migraine without aura) had immediate trial scores at the 26th percentile and delayed scores below the 25th percentile.

Normative data for the Controlled Word Association test was obtained from Benton (1973a, Lezak, 1976).

These norms were based on the sum of the three trials (F,A,S) adjusted for age, sex and education; these adjusted scores are then converted to percentiles. The sample means for each of the three groups were converted to percentiles (without adjustment) to obtain the following: 80-84th percentile - migraine with aura, 65-69th percentile - migraine without aura, and 70-74th percentile - controls. No impairment cut-off scores were provided. An examination of the individual adjusted scores revealed that two subjects (1 migraine without aura, 1 control) had scores below the 25th percentile.

No normative data was available for comparison of scores on the Buschke Selective Reminding Test. The entire sample mean indicated the 87% of the list was in long-term storage (subjects recalled the same word a minimum of two consecutive trials) after five trials, and 69% of the list was classified as consistent long-term retrieval (same word recalled on all subsequent trials) after five trials. Two migraine without aura subjects had LTS scores below 25% recall, while four subjects (migraine without aura, 2 controls) had cLTR scores below 25% recall.

The number of subjects whose performance scores fell into the impaired range/below the 25th percentile on at least two tests were as follows: migraine with aura - 2; migraine without aura - 5; and controls - 1. The number of subjects (by subject number) by cognitive test with impaired performance is presented in Table 7.

These eight subjects were further compared to the entire sample to determine if there were any significant differences in the expected direction. This subgroup was found to have significantly higher levels of trait anxiety (mean = 87.4, sd = 7.7) than the rest of the subjects (mean = 51.5, sd = 29.2), F (1,39) = 11.68, p = .0015. However, trait anxiety was found only to be significantly negatively correlated for this subgroup with dominant hand performance on the Fingertapping test, r = -.7914, $p < .05$. There were no significant differences between these groups on levels of state anxiety.

This subgroup was also found to have significantly poorer performance on most tests within the Motor Speed cluster, F (2,38) = 3.32, p = .047, the Reaction Time cluster, F (7,32) = 5.56, $p < .001$, the Psychomotor Ability cluster, F (3,30) = 4.31, p = .012, and the

Table 7

Subjects with Scores in the Impaired Range or Below the 25th Percentile by Group

	Migraine with aura (n = 14)	Migraine without aura (n = 15)	Control (n = 12)
Fingertapping			
Dominant Hand			
Jarvis & Barth (1984)			
Russell et al. (1970)			
Nondominant Hand			
Russell et al. (1970)			
Trailmaking			
Russell et al. (1970)			
A			
Digit Symbol			
Russell et al. (1970)			

Table 7 - continued

Subjects with Scores in the Impaired Range or Below the 25th Percentile by Group

	Migraine with aura (n = 14)	Migraine without aura (n = 15)	Control (n = 12)
VSAT			
Trenerry et al. (1990)			
Right			
Left	2	4	1
Associate Learning (< 1 sd below standardization group means)			
Immediate	0	1	0
Logical Memory			
Immediate			0
Delayed			0
Controlled Word Association			
(sum of 3 trials)			
Selective Reminding Test			
LTS			0
cLTR	1	1	0

Learning and Memory cluster, F (9,30) = 4.56, p = .001. In addition, a Mann-Whitney U-test revealed that Severity Index I and Severity Index II were marginally significantly higher for this subgroup, U (29) = 40.0, p = .0589, U (29) = 38.0, P = .0467. However, neither of the two Severity Indices nor Headache History were found to be significantly related to cognitive performance. Therefore, even for those subjects who had performance scores in the impaired range, there is no evidence to support the hypothesis that repeated migraine attacks may cause cumulative cognitive deficits.

The overall sample means, therefore, indicate that group cognitive performance was not indicative of cognitive impairment, and does not provide evidence in support of the main hypothesis.

An intercorrelation matrix of all of the cognitive (sub)tests was computed. Correlations in the expected directions were observed (ie. significant positive correlations within tests and between similar tests were generally observed), suggesting that performance and effort was consistent during the testing session for subjects and therefore, that the performance scores

can be considered reliable. The intercorrelation matrix is presented in Appendix H.

Summary of the significant findings

The comparisons of the migraine control subjects revealed no significant differences between groups in cognitive performance on a neuropsychological battery (in the hypothesized direction). In addition, there were no significant group differences when tests classified as "behavioural" and "cognitive" were compared, or when "left" or "right" hemispheric tests were compared using "usual headache side" as a covariate. There was no significant group difference for the number of tests performed at least one standard deviation below the sample mean (Impairment Index).

There were also no significant group differences in cognitive performance when those subjects who use medication for migraine relief or those subjects who used any medication 24 hours prior to testing were compared to those subjects who did not take or do not regularly use medication.

There were no significant group differences on levels of depression, Health Locus of Control, assessment of one's functioning and subjective mood

ratings (POMS).

Migraine with aura subjects were found only to have significantly higher levels of state anxiety than the control subjects at post-testing. The other comparisons, although not significant, revealed higher levels of state anxiety for the migraine subjects compared to the controls, both pre- and post-testing. The group means indicated that all groups had an increased level of state anxiety post-testing. In addition, the migraine subjects were found to have significantly higher levels of trait anxiety than the control subjects. However, when state and trait anxiety were used as a covariate, there were still no significant group differences in cognitive performance.

No significant correlations were observed between headache history or either of the two severity indices and cognitive performance.

When cognitive performance of the sample was compared to normative data, it was found that the sample means were not indicative of cognitive impairment. A number of individual subjects were found to have scores in the impaired range. When subjects with a minimum of two scores in the impaired range were

compared to the rest of the sample, this subgroup was found to have significantly higher trait anxiety, marginally significantly higher severity indices, and performed significantly more poorly on most of the cognitive tests. However, there still were no significant correlations between cognitive performance and headache history or severity indices for this subgroup.

Discussion

The overall results of present study do not support the hypothesis that repeated migraine attacks cause permanent and/or cumulative cognitive impairment. The present study results are generally consistent with the findings of Leijdekkers et al. (1990).

There were no significant differences between the migraine and control subjects on the Impairment Index or the Reaction Time, Motor Speed, Psychomotor Ability and Learning and Memory clusters. The significant differences observed between groups on the cognitive tests were not in the hypothesized directions. In addition, there was no evidence to suggest that medication use for migraine relief had a negative

effect on cognitive performance. This study also failed to find a significant correlation between Headache History or either of the two Severity Indices and cognitive performance. As noted by Leijdekkers et al. (1990), failure to find evidence of a relationship between cognitive performance and history or severity provides a strong argument against a relationship between repeated migraine headaches and cumulative cognitive impairment.

The migraine subjects were found to have significantly higher levels of trait anxiety than controls; state anxiety levels were consistently higher for the migraine subjects than the controls at both pre- and post-testing, but only found to be significantly higher for migraine with aura subjects than the controls at post-testing. State anxiety levels increased in all group over the testing session. However, because levels of trait and state anxiety were not found to be significantly related to any of the performance scores, and did not reveal any group differences when used as a covariate, there is no evidence to suggest that anxiety significantly negatively affects cognitive performance, at least in

the present study. In fact, some of the correlations indicated a positive relationship between anxiety and performance.

The other personality measures also revealed no significant differences between migraine and control subjects on levels of depression, Health locus of control scores, the assessment of their daily functioning and on an assessment of moods (POMS). This study did not find evidence of higher levels of depression and lower vigor levels in the migraine sample on the POMS, as found in the study by Leijdekkers et al. (1990). There was some evidence of poorer ratings in the migraine sample, although not significantly poorer, but no significant differences in cognitive performance between groups. Therefore, the extent to which subjective personality measures influence cognitive performance cannot be determined, as even significant differences in personality measures between groups did not result in significantly poorer cognitive performance.

One criticism of the Leijdekkers et al. (1990) study is the criterion used for the Impairment Index. This index reflects the number of tests for which a

subjects falls one or two standard deviations below the mean of the entire sample. The objection to this measure is that no comparison of performance was made against normative data of impaired scores/ranges. Just because a subject falls two standard deviations below the mean of its sample does not necessarily mean his/her score reflects an impaired performance. Unlike Hooker and Raskin (1986) who compared performance using normative data and computing an impairment index based on these comparisons, Leijdekkers et al. (1990) did not determine whether performance was impaired for the sample, groups or subjects. No normative comparisons were used in the Zeitlin and Oddy (1984) study as well. The present study found that the means of the entire sample for the cognitive tests were not indicative of cognitive impairment, however, individual subjects within the sample did have scores which fell within the impaired range. Further analyses of those subjects with at least two scores in the impaired range did not reveal any significant relationships between cognitive performance and Anxiety, Headache History, or Severity (Indices I, II). This observation provides even stronger evidence against the hypothesis that repeated

migraine attacks may cause cumulative cognitive impairment.

Leijdekkers et al. (1990) noted a number of differences between their study and the previous literature which may have accounted for the differences in their findings. They indicated that one possible reason for not finding cognitive impairment in their sample may have been because they used a non-clinical sample. They noted that their sample rarely sought medical attention and perhaps, experienced fewer neurologic complications and side effects than the clinic samples used in the earlier studies (Zeitlin & Oddy, 1984; Hooker & Raskin, 1986). Only 38 percent of the migraine subjects in the present study indicated they had sought medical treatment from a neurologist for their migraine headaches. However, in the study by Zeitlin and Oddy (1984) they noted that the median total number of hours of incapacitating migraine headache (Severity Index II) was 3200 hours (range 420 to greater than 19000 hours). The median total number of headache hours suffered by the present migraine sample was 17280 hours (range 1188 to 77760 hours). Based on headache hours suffered alone, it could be

argued that the present study sample was a more severe sample, but cognitive impairment was not observed. These estimates were all based on self-report data, however, and should be interpreted with some caution. In addition, the level or type (if any) of neurologic complications and/or side effects cannot be determined and therefore, compared between study samples to conclusively determine if this was a significant difference between studies.

No significant differences were observed between groups when performance on "cognitive" versus "behavioural" tests were compared. In addition, those tests found to be significant in the Zeitlin and Oddy (1984) or Hooker and Raskin (1986) studies when manually-administered but not significant in the Leijdekkers et al. (1990) study using a computer-administration, were also not found to be significantly different between groups when manually-administered in the present study. These findings, therefore, argue against the suggestion that the differences in the three previous studies may have been due to a difference in test complexity or type of test administration.

Although some personality variables were found to significantly differ between groups, there was no evidence to suggest that any personality measure had a significant negative effect on cognitive performance, even for those subjects who had performance scores in the impaired range.

Fatigue was not found to significantly affect cognitive performance. The present battery required two hours for completion, as compared to three hours in the Hooker and Raskin (1986) study and one and a half hours in the Leijdekkers et al. (1990) study. A testing session of two hours therefore, seems to be a reasonable duration for neuropsychological testing, and although longer than the Leijdekkers et al. (1990) battery, also did not seem to have a significant negative effect on performance.

The present study did not find any significant differences in performance between the two migraine groups, consistent with the results of Leijdekkers et al. (1990). Hooker and Raskin (1986) previously found some tests for which the migraine with aura group performed significantly poorer than both the migraine without aura and control subjects. Migraine without

aura subjects were not predicted to demonstrate any impairment in the Hooker and Raskin (1984) study because of the absence of neurologic disturbances during a migraine attack. In the present study, although not significantly different, it was observed that the migraine without aura group had the poorest group mean for 16 of the 21 cognitive measures. This observation and the lack of cognitive impairment in both migraine groups does not support the argument that neurologic disturbances during a headache attack will have a more negative effect on cognitive performance.

The present study did not find any evidence in support of the hypothesis that repeated migraine attacks may cause permanent and/or cumulative neurologic impairment. As noted, the only difference between the present study and the studies by Zeitlin and Oddy (1984) and Hooker and Raskin (1986) that cannot be conclusively determined is the severity of the migraine headaches. Although the estimate of total number of headache hours suffered was at minimum comparable (if not more severe) in the present study, perhaps those subjects in the two previous studies did have more serious neurologic complications and/or side

effects associated with their headaches, resulting in the observed cognitive impairment of those samples. Further research comparing a clinical versus a non-clinical sample of migraine subjects is therefore recommended, as this is the only variable suggested by Leijdekkers et al. (1990), except perhaps fatigue, which has not been replicated and ruled out as a plausible explanation for the discrepancy between the previous studies.

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Appendix A

Clinical Information Form

We are interested in assessing people who suffer from migraine headaches and those who have never had a migraine, to determine if there are common distinguishing characteristics among migraine sufferers.

I am conducting a study under the supervision of Dr. W. Melnyk, Professor of Psychology at Lakehead University, and Martyn R. Thomas, Director of the Bio-behavioural Unit at Sunnybrook Health Science Centre, as partial fulfilment of the requirements of a Master of Arts degree in Clinical Psychology.

If you agree to participate in this study, you will be asked to complete a number of questionnaires. These questionnaires will ask questions about your mood and feelings and some of your personal habits. As well, you will be asked to complete a number of tests which assess your memory, attention span and motor coordination. The test session will take approximately 2 hours to complete and may be somewhat tiring. Testing will be conducted at Sunnybrook Health Science Centre, Toronto.

Your participation is voluntary and you may withdraw from the study at any time. Should you withdraw, this will in no way jeopardize your treatment at Sunnybrook Health Science Centre.

Appendix A - continued

Clinical Information Form

There are no direct benefits of participating for yourself. All information you provide will be remain confidential and all results will be kept secure by Deborah Anderson. No individual shall be identified in any report of the results.

The findings will be made available to you, at your request, upon completion of the project.

If you would like to participate in this study, please contact Deborah Anderson at (416) 480-6100 ext. 4656, from 9:00am to 5:00pm, to arrange for an interview. Your participation would be greatly appreciated.

Sincerely,

D. Anderson, B.Sc.
M.A. Student
Lakehead University

W. Melnyk, Ph.D.
Professor of Psychology
Lakehead University

M. R. Thomas, M.A.
Director,
Biobehavioural Unit
Sunnybrook Health
Science Centre

Appendix B

Consent to Participate

My signature on this form indicates that I will participate in a study by Deborah Anderson, Dr. W. Melnyk and Martyn R. Thomas on distinguishing characteristics of migraine sufferers.

I understand the following:

1) I am a volunteer and can withdraw at any time from the study. Should I withdraw from the study, this will in no way jeopardize my treatment at Sunnybrook Health Science Centre.
2) I will be asked to complete a number of questionnaires. These will include questions which assess my mood and feelings and some of my personal habits. As well, I will be asked to complete a number of tests which assess my memory, attention span and motor coordination.
   The test session will take approximately two hours to complete and may be somewhat tiring.
4) The data I provide will remain confidential and my name will not appear on any report of the results.

Appendix B - continued

Consent to Participate

5) I will receive a summary of the study, at my request, following completion of the project.

_____ _____

Signature of Participant Date

I have explained the nature of the study to the patient and believe he/she has understood it.

_____ _____

Signature of Examiner Date

Appendix C

Screening Questionnaire

NAME: _____ SUBJECT NO. _____

DOB: _____ AGE: _____

SEX: _____

EDUCATION: _____

OCCUPATION: _____

HANDEDNESS: _____

TELEPHONE NO. (H) _____
(B) _____

PRIMARY LANGUAGE: _____

HEADACHE HISTORY

1) Do you get a headache:

never?	_____
about once a year?	_____
several times a year?	_____
about once a month?	_____
several times a month?	_____
about once a week?	_____
several times a week?	_____

Which of these statements is nearest the truth for your headaches?

My headaches are:

very mild	_____
mild	_____
not usually severe	_____
quite severe	_____
very severe	_____
terribly severe	_____
almost unbearable	_____

Appendix C - continued

Screening Questionnaire

Are your headaches on one side only:

never _____
sometimes _____
usually _____
always _____

What side are your headaches usually on? (R/L/Mixed)

4) Do your headaches have a pulsating quality? YES/NO

5) Before you get a headache do you know one is coming? YES/NO

If you do, please describe briefly what you notice:

6) Are these symptoms present during the headache as well? Y / N

How soon after this does the headache appear?

_____

8) Are there any specific triggers to your headaches? YES/NO
If YES, describe

If menstrual cycle is one, where are you in your cycle now?

9) When you have a headache do you notice any changes in your sight? YES / NO

If YES, describe briefly what you notice:

Appendix C - continued

Screening Questionnaire

10) When you have a headache do you:

lose your appetite?	_____
feel dizzy?	_____
feel sleepy?	_____
hear ringing in your ears?	_____
find that noise hurts your ears?	_____
find that light hurts your eyes?	_____
notice tingling, or any strange feeling in any part of your body?	_____
find you are aggravated by walking stairs or a similar routine activity?	_____

11) When you have a headache do you:

ever feel sick?	_____
usually feel sick?	_____
ever vomit?	_____
usually vomit?	_____
always vomit?	_____

12) How long do your headaches usually last? (# hrs)

_____

13) Hours or a day or two before your headache do you find you are:

hyperactive	_____
hypoactive	_____
depressed	_____
crave special foods	_____
yawning repetitively	_____

14) How many headaches do you usually have per month?

_____

Appendix C - continued

Screening Questionnaire

15) Which best describes your headaches:

a) I only have a headache if I pay attention to it _____
b) I have a headache but it does not interfere with my work _____
c) I have a headache, and I have difficulty concentrating _____
d) I have a headache and am unable to perform usual work, but bedrest is unnecessary _____
I have a headache and bedrest is necessary _____

16) How long have you been experiencing migraine headaches?

(# years) _____

17) Have you experienced at least 5 headaches in which:

a) headache lasted 4-72 hours? YES / NO

b) at least 2 of the following:
unilateral location _____
pulsating quality _____
moderate or severe intensity _____
(inhibits or prohibits daily activities)
aggravation by walking stairs or a similar routine physical activity

at least 1 of the following:
nausea and/or vomiting _____
photophobia or phonophobia _____

Appendix C - continued

Screening Questionnaire

18) For how long have you been experiencing headaches as those described above? _____

19) Have you had 12 headaches, as described above per year?

YES / NO

MEDICAL HISTORY

1) Have you had any serious illnesses or major surgery? YES/NO

2) Have you ever suffered any head injuries and/or been unconscious? YES / NO

Have you ever had a seizure? YES / NO

Are you currently under a doctor's care for any reason? Y/N

5) Have you ever seen a neurologist regarding your headaches? If YES, did he give you any diagnosis?

6) Are you taking any medications:

NAME	DOSE	FREQUENCY

Do you take any regular preventative medication for your migraines? YES / NO
If YES, what and what dosage?

Appendix C - continued

Screening Questionnaire

Do you have any difficulties with your sight or hearing? If YES, are you wearing corrective lenses or a hearing aid?

8) Do you consume alcohol? YES / NO
If YES, how much and how often?

9) Do you use any nonprescribed drugs? YES / NO
If YES, what type and how much how often?

Appendix D

Inclusion/Exclusion Criteria

INCLUSION CRITERIA

I. a) 18-50 years of age
   b) pain and symptom-free 48 hours before testing and at time of testing
   c) no consumption of alcohol on the evening prior to testing and day of testing

II. Headache-free control group
   a) six or less mild headaches per year (able to carry out normal work activities and no severe headaches)

III. Migraine Group
   a) fulfilling criteria for migraine without aura or migraine with aura according to the criteria of the International Headache Society (1988)
   b) minimal history of migraine two years
   c) at least three headache days per month

EXCLUSION CRITERIA

I. Migraineurs who take regular preventative medication for their headaches.

II. Any subjects who have been given a previous diagnosis of central nervous system disease/trauma, cranial nerve disease/trauma, peripheral nervous system disease/trauma, systemic diseases or extracranial pain conditions will not be included (see below)

III. Headache other than defined by the inclusion criterion

IV. a) conversion cephalgia
   b) major depression
   c) primary thought disorder
   d) substance abuse

Appendix D - continued

Inclusion/Exclusion Criteria

Any subjects who are identified during testing as having an IQ below "low average" based on the Vocabulary subtest of the Wechsler Adult Intelligence Scale-Revised (1981) will be excluded from the results to avoid contamination of the data due to baseline intelligence

VI. Subjects who are found to have sensory deficits (ie. vision, hearing not correctible with lenses, hearing aids, etc.) will not be included.

VII. Only subjects whose primary language is English will be included. Appendix B

EXCLUSION DISORDERS

I. Central nervous system disease/trauma
   a) seizure history
   b) head injury with loss of consciousness
   c) cerebrovascular occlusive disease (clotting of brain vessels)

II. Cranial nerve disease/trauma
   a) trigeminal neuralgia (severe sharp pain along opthamalic, mandibular or maxillary nerves)
   b) glossopharyngeal neuralgia (severe sharp pain involving the taste bud areas)
   c) postherpetic neuralgia

III. Peripheral Nervous System Disease
   a) motor/sensory damage to upper extremities
   b) thoracic outlet syndrome (characterized by inflammation of the nerves of the arm)
   c) carpal tunnel syndrome
   d) peripheral vascular disease (disease of the arteries and veins of the extremities)

Appendix D - continued

Inclusion/Exclusion Criteria

IV. Systemic Disease
a) juvenile onset diabetes
b) chronic obstructive pulmonary disease
c) renal disease
d) chronic alcohol abuse
e) opiate dependence

Extracranial Pain Conditions
a) dental pain
b) temporo-mandibular joint disease
c) otolaryngologic disease
d) cervical disk disease
e) ocular disease

Appendix E

Ad Hoc Committee Classification of Migraine Headache

MIGRAINE WITHOUT AURA

A. At least 5 attacks fulfilling B-D

B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated).

Headache has at least two of the following characteristics:

1. Unilateral location
2. Pulsating quality
3. Moderate or severe intensity (inhibits or prohibits daily activities)

Aggravation by walking stairs or similar routine physical activity).

During headache at least one of the following:

1. Nausea and/or vomiting
2. Photophobia and phonophobia

At least one of the following:

1. History, physical- and neurological examinations do not suggest one of the disorders listed in groups 5-11

Appendix E - continued

Ad Hoc Committee Classification of

Migraine Headache

History and/or physical- and/or neurological examinations do suggest such disorder, but it is ruled out by appropriate investigations
Such disorder is present, but migraine attacks do not occur for the first time in close temporal relation to the disorder

MIGRAINE WITH AURA

A. At least 2 attacks fulfilling B

B. At least 3 of the following 4 characteristics:

1. One or more fully reversible aura symptoms indicating focal cerebral cortical- and/or brain stem dysfunction
   At least one aura symptom develops gradually over more than 4 minutes or, 2 or more symptoms occur in succession
   No aura symptom lasts more than 60 minutes.
   If more than one aura symptom is present, accepted duration is proportionally increased

Appendix E - continued

International Headache Committee Migraine Classification Criteria

Headache follows aura with a free interval of less than 60 minutes (it may also begin before or simultaneously with the aura)

Aura symptoms of the following type:

a. Homonymous visual disturbance

b. Unilateral paresthesias and/or numbness

c. Unilateral weakness

d. Aphasia or unclassifiable speech difficulty

At least one of the following:

History, physical- and neurological examinations do not suggest one of the disorders listed in groups 5-11

History and/or physical- and/or neurological examinations do suggest such disorder, but it is ruled out by appropriate investigations

Such disorder is present, but migraine attacks do not occur for the first time in close temporal relation to the disorder

Appendix F

Assessment of Own Functioning Inventory

Instructions: Please answer each of the following questions by placing a check next to the response which most accurately describes the way you have been recently.

How often do you forget something that has been told you within the last day or two?

(M-1)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

How often do you forget events which have occurred in the last day or two?

(M-2)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

How often do you forget people whom you met in the last day or two?

(M-3)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

Appendix F - continued

Assessment of Own Functioning Inventory

How often do you forget things that you knew a year or more ago?

(M-4)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

How often do you forget people whom you knew or met a year or more ago?

(M-5)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

How often do you lose track of time, or do things either earlier or later than they are usually done or are supposed to be done?

(M-6)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

Appendix F - continued

Assessment of Own Functioning Inventory

How often do you fail to finish something you start because you forgot that you were doing it? (Include such things as forgetting to put out cigarettes, turn off the stove, etc.)

(M-7)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

How often do you fail to complete a task that you start because you have forgotten how to do one or more aspects of it?

(M-8)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

How often do you forget things that you are supposed to do or have agreed to do (such as putting gas in the car, paying bills, taking care of errands, etc.)?

(M-9)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

Appendix F - continued

Assessment of Own Functioning Inventory

10. How often do you have difficulties understanding what is said to you?

(LC-1)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

11. How often do you have difficulties recognizing or identifying printed words?

(LC-2)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

12. How often do you have difficulty understanding reading material which at one time you could have understood?

(LC-3)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

Appendix F - continued

Assessment of Own Functioning Inventory

13. When you speak, are your words indistinct or improperly pronounced?

(LC-4)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

Note: If this happens, how often do people have difficulty understanding what words you are trying to say?

(LC-5)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

14. How often do you have difficulty thinking of the names of things?

(LC-6)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

Appendix F - continued

Assessment of Own Functioning Inventory

15. How often do you have difficulty thinking of the words (other than names) for what you want to say?

(LC-7)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

16. When you write things, how often do you have difficulty forming the letters correctly?

(LC-8)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

17. Do you have more difficulty spelling, or make more errors in spelling, than you used to?

(LC-9)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

Appendix F - continued

Assessment of Own Functioning Inventory

18. How often do you have difficulty performing tasks with your right hand (including such things as writing, dressing, carrying, lifting, sports, cooking, etc.)?

(Hands-1)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

19. How often do you have difficulty performing tasks with your left hand?

(Hands-2)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

20. How often do you have difficulty feeling things with your right hand?

(Percept-1)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

Appendix F - continued

Assessment of Own Functioning Inventory

21. How often do you have difficulty feeling things with your left hand?

(Percept-2)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

22. Lately, do you have more difficulty than you used to in seeing all of what you are looking at, or all of what is in front of you (in other words, are some areas of your vision less clear or less direct than others)?

(Percept-3)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

23. How often do your thoughts seem confused or illogical?

(CI-1)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

Appendix F - continued

Assessment of Own Functioning Inventory

24. How often do you become distracted from what you are doing or saying by insignificant things which at one time you would have been able to ignore?

(CI-2)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

25. How often do you become confused about (or make a mistake about) where you are?

(CI-3)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

26. How often do you have difficulty finding your way about?

(CI-4)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

Appendix F - continued

Assessment of Own Functioning Inventory

27. Do you have more difficulty now than you used to in calculating or working with numbers (including managing finances, paying bills, etc.)?

(CI-5)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

28. Do you have more difficulty now than you used to in planning or organizing activities (ie., deciding what to do and how it should be done)?

(CI-6)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

29. Do you have more difficulty now than you used to in solving problems that come up around the house, at your job, etc.? (In other words, when something new has to be accomplished, or some new difficulty comes up, do you have more trouble figuring out what should be done and how to do it?)

(CI-7)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

Appendix F - continued

Assessment of Own Functioning Inventory

30. Do you have more difficulty now than you used to in following directions to get somewhere?

(CI-8)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

31. Do you have more difficulty now than you used to in following instructions concerning how to do things?

(CI-9)
( ) almost always
( ) very often
( ) fairly often
( ) once in a while
( ) very infrequently
( ) almost never

Appendix G

Pain Self-Rating Scale

Please place a mark on the line at a point representing the severity of the pain you usually experience during a headache.

Appendix H

Intercorrelations of the Cognitive Tests

Dominant,	Nondominant	0.6344**
	Control A	0.4041**
Nondominant,	Logic 1	0.3531*
	Control A	0.5466**
	Control S	0.3864*
Pasat 1,	Pasat 2	0.6645**
	Pasat 3	0.7111**
	Pasat 4	0.4987**
	Control F	-0.3301*
Pasat 2,	Pasat 3	0.7373**
	Pasat 4	0.4163**
	Logic 1	-0.4298**
	Logic 2	-0.3723*
Pasat 3,	Pasat 4	0.6817**
	Logic 1	-0.3946*
	Logic 2	-0.3704*
	Control F	-0.3269*
	Control S	-0.3936*
Pasat 4,	Trail B	0.3848*
	Verbal 1	-0.4147**
	Logic 1	-0.3433*
	Logic 2	-0.3542*
	Control F	-0.3656*
	LTS	-0.5162**
	cLTR	-0.3827*
Trail A,	Trail B	0.4302*
	VsatLT	-0.4014*
	VsatTOT	-0.3692*
Trail B,	Verbal 1	-0.3282*
	Verbal 2	-0.3902*
	LTS	-0.3429*

Appendix H - continued

Intercorrelations of the Cognitive Tests

Verbal 1,	Verbal 2	**0.4400****
	LTS	**0.5304****
	cLTR	**0.5266****
Verbal 2,	LTS	**0.3789***
	cLTR	**0.4689****
Logic 1,	Logic 2	**0.8308****
	DigitSy	**0.3396***
	LTS	**0.5261****
	cLTR	**0.3557***
Logic 2,	LTS	**0.5934****
	cLTR	**0.3509***
VsatLT,	VsatRT	**0.9349****
	VsatTOT	**0.9827****
	DigitSy	**0.5699****
VsatRT,	VsatTOT	**0.9841****
	DigitSy	**0.6153****
VsatTOT,	DigitSy	**0.5972****
Control F,	Control A	**0.4707****
	Control S	**0.5267****
Control A,	Control S	**0.5166****
LTS,	cLTR	**0.7482****

**p < .01. *p < .05.

***NOTE: All correlations presented are non-redundant
See legend for explanation of abbreviations

Appendix H - continued

Intercorrelations of the Cognitive Tests

Legend:

Dominant, Nondominant	Hands, **FINGERTAPPING**
Logic 1, Logic 2	Immediate, Delayed Trials, **LOGICAL MEMORY**
Control F,A,S	Trials, **CONTROLLED WORD ASSOCIATION TEST**
Pasat 1,2,3,4	Presentation rates: 2.4s, 2.0s, 1.6s, 1.2s **PACED AUDITORY SERIAL ADDITION TEST**
Trail A, B	Trials, **TRAILMAKING TEST**
Verbal 1,2	Immediate, Delayed Trials, **ASSOCIATE LEARNING**
DigitSy	Digit Symbol, **WAIS-R**
VsatLT, RT, TOT	Left, Right, Total scores **VISUAL SEARCH AND ATTENTION TEST**
LTS, cLTR	Long-term storage, consistent long-term retrieval, **BUSCHKE SELECTIVE REMINDING TEST**