Neuropsychological Functioning of Migraine Patients With- and Without Aura, and Cerebral Hemisphere Laterality

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NEUROPSYCHOLOGICAL FUNCTIONING OF MIGRAINE PATIENTS WITH- AND WITHOUT AURA, AND CEREBRAL HEMISPHERE LATERALITY

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Concordia University, 2005

Differences in cognition between patients with migraines and healthy control subjects have been documented by several researchers, principally in the areas of attention, memory, and motor function. Patients with aura (MA) are more often reported to have interference with normal cognitive functioning and are thought to have a more severe neurological condition than do patients without aura (MO). We compared the cognitive profiles of 29 right-handed patients, recruited at the Montreal Neurological Hospital, and diagnosed with hemicranial MA and MO to that of 10 healthy control subjects (NC). Diagnosis was made according to the International Headache Society guidelines by a neurologist. From a personality perspective, higher levels of self-consciousness were documented in MA and M_{Left} than in NC and MO ($F = 2.67$, $p < .05$). NC's response styles were more original while patients preferred more conservative ones ($F = 4.65$, $p < .01$). Examination of cognitive data from an extensive neuropsychological battery was performed. MA performed worse than NC and MO on a General Cognitive Index ($F = 2.72$, $p < .05$), Full Scale ($F = 6.10$, $p < .001$) and Verbal ($F = 5.48$, $p < .01$) IQ. Verbal IQ was also lower for MO than

for NC ($F = 10.69$, $p < .001$). Compared to NC and left-hemisphere migraines (M_{Left}), right-hemisphere migraines (M_{Right}) demonstrated reduced attention ($F = 3.96$, $p < .05$), poorer constructional abilities ($F = 4.38$, $p < .05$), and lower visuo-spatial memory ($F = 3.92$, $p < .05$). M_{Right} performed less well on executive functioning tasks ($F = 2.65$, $p = .05$). M_{Left} was associated with lower Full Scale IQ ($F = 8.34$, $p < .001$) and Verbal IQ ($F = 7.89$, $p < .001$). MA (Right Hand: $F = 3.90$, $p < .05$; Left Hand: $F = 4.10$, $p < .05$) had poorer motor skills than NC. M_{Right} (Left Hand: $F = 3.61$, $p < .05$) showed additional motor slowness. Thus, presence of aura and hemisphere lateralization of migraine headache can affect the cognitive and personality profiles of patients with migraine.

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I dedicate this dissertation to my fiancé Jon and my nephew Alex for standing by, encouraging, and helping me complete my work.

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INTRODUCTION

Accounts of migraine originate from ancient Mesopotamia and Egypt (Andrews, 1998). The Ebers Papyrus, dated around 1500 BC, is an Egyptian medical treatise that describes headaches as "sickness of the half of the head" and includes a passage concerning the treatment of migraine (Andrews, 1998; Medicine in Ancient Egypt, n.d.). Hippocrates (460–375 BC) was the first to describe a collection of symptoms that included aura, pain, and vomiting as part of a singular disorder and not a punishment sent by the gods, however, he did not specify a name for this health problem. Five hundred years later, Galen of Pergamon (AD 131–201) proposed the name "hemikrania" to reflect unilateral head disease. This word evolved over time into the Latin "hemigrainea," followed by "migranea," and finally the modern French designation of migraine (Andrews, 1998).

Migraine along with tension-type headaches, cluster headaches, and other trigeminal autonomic cephalalgias are classified as primary headaches. Migraine represents a chronic neurological disorder in which the majority of patients report pain localization to one side of the head. A sub-population of migraine patients experience well-defined premonitory symptoms collectively known as the migraine aura that encompass sensory and/or motor disturbances, as well cognitive features such as speech,

attention, and concentration difficulties. In migraine with aura (MA) the aura dissipates in about one hour and is followed by the headache pain (Hooker & Raskin, 1986).

Migraine without Aura

To fulfill the International Headache Society (IHS, 1988 and 2004) diagnostic criteria for migraine without aura, patients must have experienced a minimum of five attacks lasting for 4 to 72 hours untreated or treated unsuccessfully with medication. Headaches must have two or more of the four following characteristics: unilateral location; pulsating quality; moderate or severe intensity (defined as sufficiently intense to inhibit or prohibit daily activities); and be aggravated by routine physical activity. In addition, diagnosis requires the presence of accompanying symptoms of nausea and/or vomiting, and/or photophobia and phonophobia.

Migraine with Aura

As per the IHS definition, migraine with aura is a spontaneously recurring neurological disorder of unknown origin (i.e., idiopathic) characterized by aura symptoms that are clearly generated in the cerebral cortex or the brain stem. Aura represents a combination of focal neurological symptoms that develop over a span of 5–20 minutes and can last up to 60 minutes. The diagnostic criteria for migraine with aura require a minimum of two attacks comprised of at least three of the following four characteristics: one or more symptoms indicating focal cortical or brain stem dysfunction

that disappear completely such that no one symptom lasts more than 60 minutes; at least one aura symptom develops gradually over more than four minutes or two or more symptoms occur in succession; and if headache does not begin prior to or concurrent with the aura, it follows within 60 minutes. To establish a diagnosis of migraine with typical aura, at least one of the following aura features is required: homonymous visual field disturbance; unilateral paresthesias and/or numbness; unilateral weakness; aphasia or unclassifiable speech difficulty. The aura is most frequently a visual cortex event that starts as a bright spot at the center of the visual field that then enlarges toward the periphery in the form of a curved, zigzagging line. Finally, the aura develops into what has been called the 'fortification spectrum' because it resembles the fortification walls of medieval cities (Lauritzen, 2001). The first detailed depictions of visual aura have been provided by Lashley (1941) who defined them as localized areas of diminished vision bordered by shimmering colored lights. In rare instances, it is possible to experience aura without the ensuing migraine pain.

Applying the IHS criteria for migraine, incidence rates of approximately 17.6% in women and 6% in men in the United States are reported (Lipton & Bigal, 2005; Stewart, Lipton, & Liberman, 1996; Lipton & Stewart, 1993; Breslau, Davis, & Andreski, 1991; Linet et al., 1989). A nationwide survey of the German population quotes migraine incidence rates of 15% in women and 7% in men (Göbel, Petersen-Braun, & Soyka, 1994), while in France, 12% of women, and 4% of men are thought to have migraine (Henry et al., 1992). In Canada, incidence rates are 21.9% in women and 7.4% in men (O'Brien, Goeree, & Streiner, 1994). The presence of a 3 to 1 ratio of migraine in

women versus men has yet to be explained. It has been hypothesized, that the greater incidence among women may be related to the female hormonal cycle as well as to differences in the distribution and retention of brain serotonin levels in males and females (Aubé & Beaulieu, 2004). The latter hypothesis is linked to the demonstration of the effectiveness of a class of serotonin agonists known as triptans for the acute treatment of migraine.

The severity of a medical disorder is determined by taking into account the degree of disability, duration of illness, and the extent of negative psychological and social influences. Patients with migraine describe increased levels of perceived difficulties in the completion of daily activities and a reduced quality of life on self-report questionnaires. Pesa & Lage (2004) evaluated the medical costs associated with regular checkups for healthy subjects versus the medical costs of adults with migraine (adults with migraine, n = 5997; matched healthy subjects n = 5666) and children (children with migraine n= 473; matched healthy subjects n = 445) with migraine. This investigation found that adult migraine patients had significantly higher total direct medical costs (7,089 USD versus 2,923 USD) and children with migraine incurred an average of 4,272 USD in total direct medical costs while the costs for healthy control children averaged only 1,400 US Dollars. Therefore, when compared to healthy control subjects, Pesa & Lage report that the direct medical costs associated with a diagnosis of migraine are 2.4 times higher in adults and 3 times higher in children. Migraine is a relatively common disorder and has a significant impact on the lives of the individuals affected and on society.

Despite important scientific progress regarding its pathophysiology, migraine remains a collection of disorders, each with a specific set of symptoms and diagnostic criteria that have yet to be fully understood. Etiological perspectives have evolved from the belief that migraines were the expression of the caprices of the Deities, the result of harmful vapors that diffused into the brain from other parts of the body, to a vascular theory whereby migraines were induced by extra-cranial arterial dilatation. Contemporary views of migraine pathophysiology, however, provide convincing support for a central nervous system origin of migraine (Gorji et al., 2001; Strong et al., 2002).

Migraine Pathophysiology

A combination of genetic factors causing specific biological or physical abnormalities and environmental factors have been hypothesized to underlie migraine. Typical research targets have included measures of cerebral blood flow, monitoring of hormonal changes in the central nervous system, and recordings of cellular electrical imbalances.

For many years, the generally accepted mechanism underlying migraine generation has implicated a component of the trigeminovascular system (Wolff, 1963). According to this vascular hypothesis, the headache phase of migraine with- and without aura is associated with the painful dilatation of large extra- or intracranial vessels (Hardebo, 1991). It is hypothesized that when present, the aura component is characterized by visual, perceptual, sensory, or motor symptoms that are a consequence

of insufficient cerebral perfusion resulting from cerebral arterial vasoconstriction and/or blood platelet aggregation. Several clinical arguments have been used to support a vascular account for migraine. For example, the pulsating quality of the pain in migraine resembles that of the headaches present in vascular diseases such as stroke, subarachnoid hemorrhage, and arterial hypertension. The finding that ergotamine, a drug that constricts cerebral arteries without decreasing cerebral blood flow (CBF) could treat vascular headaches effectively (Tfelt-Hansen, Sperling, & Andersen, 1991) was also taken to support the migraine vascular theory. This latter argument, however, has been significantly weakened by studies linking migraine to a steady decline in regional CBF (rCBF). The reduction in rCBF was shown to follow the cortical surface in a pattern consistent with arteriolar, but not arterial blood supply (Olesen, Tfelt-Hansen, Henriksen, & Larsen, 1981; Lauritzen, 1987; Olesen, 1981). Lauritzen (1994) observed that arterial vasoconstriction severe enough to elicit an rCBF decline would have to be associated with a compensatory dilatation of arterioles leading to a mixed pattern of decreases and increases in rCBF. Since this mixed pattern is not present in migraine, a strictly vascular model cannot provide a full account of migraine pathophysiology.

Another explanation of migraine pathophysiology proposes a neurogenic origin. Clinical endorsement is provided by the similarity between the unprovoked, stereotyped, repetitive, and transient nature of the brain disturbance in both migraine and epilepsy, a central nervous disorder (Gowers, 1907; Post & Silberstein, 1994). Investigations supporting the view that the same primary neuronal and secondary hemodynamic events precede migraine, irrespective of the presence or absence of aura, provide additional data

in favor of a central nervous system origin for migraine. These studies contend that migraine is triggered by a cortical spreading depression-like phenomenon. Cortical spreading depression (CSD) is characterized by rapid and almost complete neuronal depolarization that is accompanied by the redistribution of ions between intra- and extracellular membrane compartments and was first described in rabbits by Leão (1944).

Unequivocal demonstration of the CSD phenomenon in humans has proven challenging; however, recent data using electrocorticogram recordings have revealed CSD in the human brain (Gorji et al., 2001; Strong et al., 2002). Experimental manipulations have demonstrated that CSD occurs a few minutes after the interruption of the blood flow or the oxygen supply to the brain and it evolves as a regenerative process that propagates in a wave-like form through the grey matter (Somjen, 2001). CSD is initiated as a wave of intense excitation in the primary visual cortex that progresses anteriorly towards parietal and temporal brain areas at a rate of about 2-3 mm/min. In migraine, stimulation overload to a low threshold cortical area is believed to initiate a wave of spreading excitation that is responsible for generating the aura phase (Olesen et al., 1981; Lauritzen, 1987). In migraine without aura (MO), the events associated with the aura phase are present, but deemed clinically silent. In such a case of spontaneous headache, Woods et al. (1994) described a bilateral spreading depression-like wave starting at the occipital pole and advancing into the anterior cortical regions. Cao et al. (2002) have reported spreading suppression of neural activity in the occipital cortex before the onset of headache in migraine patients with or without aura. Although the central nervous system hypothesis provides an excellent account of the aura phase of

migraine, it does not adequately explain the onset of the headache pain associated with migraine.

Another theory, the neurovascular model, unifies the vascular and neurogenic approaches in an attempt to explain migraine pathophysiology. According to this view, higher cortical centers stimulate the central nervous system (CNS) end of the trigeminal sensory axon setting in motion the migraine cascade that starts with the aura phase, and is followed by the migraine phase. The aura phase is present at the beginning of all migraine attacks, but remains clinically silent in MO. Giammarco, Edmeads, & Dodick proposed that the aura phase is triggered at the front of the CSD wave where the nerve cells depolarize, and is followed by changes in blood flow lasting for several hours (1998). Because the rate of propagation of the visual aura calculated by Lashley (1941) to be approximately 2–3 mm/min, corresponded to that of CSD, Milner (1958) hypothesized that CSD might be responsible for the occurrence of the migraine aura.

In 1984, Moskowitz remarked that not only do visual auras and CSD share similar rates of propagation, but also the duration of aura symptoms might reflect the time required for the CSD wave to propagate to- and activate pain-triggering sources. Thus, the headache phase of migraine was proposed to be the consequence of a series of events set in motion by CSD. Laurizen (1994) suggested that the intracranial initiation of the headache phase of migraine requires the activation of pain-sensitive fibers found in the ventral surface of the brain. According to the neurovascular model, CSD activates the trigeminal nucleus caudalis causing a trigeminal inflammation that, in turn, activates

pain-sensitive fibers of the trigeminal nociceptive system manifested behaviourally as the headache pain (Bolay et al., 2002; Choudhuri et al., 2002; Moskowitz et al., 1993). Cao et al. (1999) concluded that spreading depression is correlated with the onset of migraine, independent of whether aura symptoms precede the attacks, and proposed that the vasodilatation accompanying the initial CSD might be associated with the induction of the headache pain.

Migraine and Neurotransmitters

Several neurotransmitters including gamma-aminobutyric acid (GABA), glutamic acid, serotonin, and dopamine have been investigated as potential modulators of migraine. A neurotransmitter is a chemical messenger used by neurons to communicate in one direction with other neurons. It has been hypothesized that the headache phase of migraine may develop as the result of abnormal interactions between neurotransmitters and neuronal receptors (Limmroth, Cutrer, & Moskowitz, 1996; Moskowitz, Reinhard Jr, Romero, Melamed, & Pettibone, 1979).

GABA

GABA and glutamic acid are key inhibitory and excitatory neurotransmitters of the central nervous system and are responsible for modulating pain threshold and neuronal excitability. It has been hypothesized that a deregulation of GABA may influence significantly the incidence of migraine attacks, while increased levels of

glutamic acid may correspond to a biochemical marker of neuronal hyperexcitability that may underlie the migraine aura (D'Andrea, Granella, Cataldini, Verdelli, & Balbi, 2001; Welch, Chabi, Bartosh & Meyer, 1975). Available biochemical information suggests that GABA mechanisms play an important role in the pathophysiology of migraine, such that increases in GABA metabolism have a compensatory role that lead to a reduction in the number of migraine attacks (Marukawa, Shimomura, & Takahashi, 1992). Pharmacological evidence also supports the hypothesis that GABA increases in the gabaergic synaptic cleft lead to enhanced inhibitory neurotransmission (Silberstein, 1996). Valproate, a gabaergic drug is well established for the prophylactic and acute treatment of migraine. Abnormal release of glutamate leads to neuronal hyperexcitability, which has been hypothesized to play a key role in the propagation of CSD (D'Andrea, Cananzi, & Welch, 1989; Welch, D'Andrea, Tepley, Barkley, & Ramadan, 1990).

Serotonin

The discovery of improved medications for both the prophylaxis and abortion of migraine attacks have directed research toward the possible role of serotonin receptors and antagonists for explaining migraine pathology. Serotonin serves predominantly as an inhibitory neurotransmitter whose main center is located in the raphae nuclei in the brainstem. Neurogenic inflammation and pain diffusion are two of the processes that have been strongly implicated in migraine pain and are blocked by the activation of 5-HT receptors (Leone, Rigamonti, D'Amico, Grazzi, et al., 2001). Migraine sufferers have a

lower 5-HT systemic content of platelets and this may predispose them to develop headaches (Evers, Quibeldey, Grotemeyer, Suhr et al., 1999; Ferrari & Saxena, 1993). Ferrari & Saxena (1993) proposed that the activation of vascular serotonin receptors might alleviate the headache without influencing the processes that prompt the migraine cascade. Research directed at the role of serotonin in migraine pathology is based on the discovery of triptans, a class of serotonin (5-HT) agonists that are currently the most effective migraine-aborting drugs available.

Dopamine

Clinical, pharmacological, and genetic evidence supports the presence of a hypersensitive dopaminergic system in migraine. Pharmacological evidence supporting a hypersensitive dopamine system in migraine comes from investigations of the efficacy of dopamine agonist medications such as haloperidol, procholorperazine, domperidone, and chloropromazine. These latter drugs have all been found to be effective in the treatment of migraine (Kelly, Ardagh, Curry, D'Antonio, & Zebic, 1997; Peroutka, 1997; Yealy, 1994). Given the increased prevalence of migraine in members of the same family, several studies have applied molecular genetic analysis focusing on the dopamine D2 receptor as a candidate gene for understanding migraine pathology (Cherchi, Stochino, Piccardi, & Del Zompo, 2001; Del Zompo, Cherchi, Palmas, Ponti, et al., 1998; Palmas, Cherchi, Stochino, Congiu, et al., 2000; Peroutka, Wilhoit, & Jones, 1997). Blau (1992) observed that the initial phase of migraine was associated with changed sensory perception that may be associated with dopamine deregulation. Nausea and vomiting,

two symptoms commonly present in migraine, are regulated in part by the activation of the dopaminergic system via dopamine D2 receptors found in the nucleus of the solitary tract in the brainstem (Del Zompo, Lai, Loi, & Pisano, 1994).

Migraine and Medication

The partial understanding of migraine pathophysiology and the underlying mechanisms that lead to migraine attacks continue to provide substantial challenges in the development of effective therapies. Pharmacological interventions for migraine include medications taken to treat attacks as they happen (acute treatment) and prophylactic medications taken daily whether or not a headache is present. Prophylactic treatments are classified in five broad categories and are prescribed to diminish the frequency and severity of the attacks. The classification of preventive drugs depends on their proven efficacy, safety profile, the presence of significant adverse events, and clinical experience (Canadian Pharmacists Association, 2001; Edwards, Glantz, Shea, Norton, et al., 2000; Lipton, Silberstein, Saper, Bigal, et al., 2003; Medline Plus, 2005; Potter, Hart, Calder, & Storey, 2000; Reveiz-Herault, Cardona, Ospina, & Carrillo, 2003). Medications with demonstrated efficacy include GABA inhibitors (e.g., divalproex sodium), beta-blockers acting as 5-HT2 agonists (e.g., propranolol and timolol), and tricyclic antidepressant amitriptyline (Herring & Kuritzky, 1992; Jensen, Brinck & Olesen, 1994). Agents with limited or no proven efficacy include alpha-agonists (e.g., clonidine), 5-HT antagonists (e.g., dihydroergocryptine), calcium-channel blockers (e.g., nifedipine), NSAIDs (e.g.,

indomethacin), and anti-epileptic drugs such as carbamazepine and vigabatrin (Silberstein & Freitag, 2003).

Acute treatment includes non-specific drugs such as analgesics and nonsteroidal anti-inflammatory medications (e.g., aspirin, acetaminophen, ibuprophen, and naproxen), which can provide effective treatment if taken in an adequate dose at the onset of the headache component of the attack (Goadsby, Lipton, & Ferrari, 2002). Generalized vasoconstrictors including ergotamine and dihydroergotamine have a long history of use and are recommended for patients experiencing prolonged or very frequent attacks (Quality Standards Subcommittee of the American Academy of Neurology, 1995; Tfelt-Hansen, Saxena, Dahlöf, Pascual, et al., 2000). Triptans are used to specifically treat acute migraine attacks; they are serotonin agonists that activate the 5-HT1 receptors with three potential mechanisms of action: cranial vasoconstriction; peripheral neuronal inhibition; inhibition of the activity of second-order neurons of the trigeminocervical complex (Gardener, 1999; Goadsby, Lipton, & Ferrari, 2002; van der Post, Schram, Schoemaker, Pieters, et al., 2002; Waeber & Moskowitz, 2003). Unpleasant side effects encompass confusion, agitation, dizziness, and somnolence in 4 to 9 % of users (Ferrari, Roon, Lipton, & Goadsby, 2001). Cognitive effects are consistent with enhanced impulsivity evident in diminished information processing capacity and reduced decision-taking abilities; they induce slight, but significant reduction in reaction times and a decline in correct word identification (Kleidienst-Vanderbeke, 1998; Proiettini-Cecchini, Afra, & Schoenen, 1997; Read & Parsons, 2000).

Migraine and Studies of Cerebral Activation

Studies of cerebral activity in patients with migraine have been directed at the elucidation of the underlying mechanisms and the potential deficits associated with a diagnosis of migraine. Evoked potential measures (ERP), transcranial magnetic stimulation (TMS), and neuroimaging have been used to record the activity of various brain regions of patients with migraine with- and without aura.

Evoked Potential Studies

In light of their non-invasive nature and ability to detect functional abnormalities, evoked-potentials (ERPs) have been used extensively over the past 30 years in studies of migraine. Although almost all sensory modalities have been investigated, the auditory and visual modalities are the ones most frequently stimulated. A large body of research pertains to cognitive evoked potentials such as contingent negative variation (CNV) and P300 and several interictal and ictal abnormalities have been reported. However, results of evoked potential investigations remain contradictory (Ambrosini, de Noordhout, Sandor, & Schoenen, 2003). Some studies of visual pattern-reversal have reported normal evoked potential amplitudes (Afra, Cecchini, Sandor, & Schoenen, 2000; Sener, Haktanir, & Demirci, 1997). Polich, Ehlers, & Dalessio (1986) reported decreased amplitudes, while others have found increased amplitudes between attacks (Kennard, Gawel, Rudolph, & Rose, 1978; Mariani, Moschini, Pastorino, Rizzi, et al., 1988). P100

amplitudes were found to be either reduced or enhanced on the side of aura (Shibata, Osawa, & Iwata, 1997; Tagliati, Sabbadini, Bernardi, & Silvestrini, 1995).

Despite incongruous findings, data from investigations applying repetitive event related stimulation show that a lack of habituation is present in migraine patients as compared to healthy control subjects. Habituation is a complex phenomenon believed to depend on cortical excitability and to serve as a protective mechanism against over-stimulation. Habituation represents a basic form of learning that allows an individual to ignore superfluous information following repeated presentation of stimuli and is associated with selective information processing abilities (Kandel, 1992). Ambrosini et al. (2003) have suggested that a lack of habituation might be the result of decreased cortical activation associated with cortical hypo-excitability. It has been further hypothesized that the lack of habituation found in patients with migraine could activate the trigeminovascular cortical system that would trigger the headache pain (Ambrosini et al., 2003; Schoenen, 1994). In healthy control subjects, repetitive presentation of visual stimuli typically results in a decrease in the amplitude of the N1-P1 and P1-N2 brainwave components. However, since these components were found to remain unchanged or increase in amplitude in patients tested during migraine-free intervals it has been proposed that this may represent another example of a lack of habituation associated with a migraine diagnosis (Afra et al., 1998; Schoenen et al., 1995).

Transcranial Magnetic Stimulation Studies

Transcranial magnetic stimulation provides a viable approach to understand how migraine may be elicited intracranially. When compared to evoked potential recordings, TMS has the advantage of directly influencing the underlying excitability of the human cortex, and migraine investigations applying TMS have targeted the motor and visual cortices. Despite contradictory findings, there is compelling evidence to suggest that cortical excitability is modified in migraine patients between attacks. In general, the discrepancies between studies are due to differences in methodology, the patient population, and in the case of visual stimulation, to the poor reliability of phosphene reporting (Afra, 2000; Afra, Mascia, Gérard, Maertens de Noordhout, et al., 1998; Peatfield, Gawel, & Clifford Rose, 1981).

Evidence from motor cortex TMS suggests that the cerebral cortex and possibly subcortical structures are interictally dysfunctional in migraine with- and without aura (Ambrosini & Schoenen, 2003). Some investigators have shown that the electrophysiological abnormalities in patients with migraine had the tendency to normalize just before and during the attacks (Ozturk, Cakmur, Donmez, Yener, Kursad, & Idiman, 2002; Schoenen, Ambrosini, Sandor, & Maertens de Noordhout, 2003). These data were taken to favour ERP data pointing to a lack of habituation in migraine and to support the hypothesis that migraine is associated with reduced motor cortex excitability.

Other investigators, however, associate a diagnosis of migraine with increased interictal cortical excitability (Van der Kamp, van den Brink, Ferrari, & van Dijk, 1996).

Van der Kamp et al. (1996) reported increased motor evoked potential (MEP) amplitudes in migraine patients, irrespective of presence or absence of aura symptoms or headache laterality. MEPs were demonstrated to correlate positively with the attack frequency, which lead to the conclusion that cortical hyperexcitability is correlated to migraine diagnosis and is more pronounced when aura symptoms are present.

Transcranial magnetic stimulation (TMS) induces visual phosphenes with stimulation of the primary visual cortex. Phosphenes are visual illusions that represent the most common phenomena present in 82 to 90% of patients diagnosed with MA (Peatfield et al., 1981; Rasmussen & Olesen, 1992). The excitability of the visual cortex can be evaluated in individual subjects by determining the threshold for phosphene induction and subsequently group differences can be estimated by calculating the incidence of phosphenes at maximal stimulation (Afra, 2000). The data accumulated thus far, are mixed. Some studies found no differences in phosphene threshold for TMS between patients with migraine and healthy control subjects (Brighina, Piazza, Daniele, & Fierro, 2002; Valli, Cappellari, Zago, Ciammola, et al., 2002). Other studies found significantly lower rates of phosphene occurrence in MA following TMS as compared to healthy control subjects (Afra, et al., 1998; Aggugia, Zibetti, Febbraro, & Mutani, 1999). Bohotin and colleagues (2002) applied a habituation paradigm to assess the excitability of the occipital cortex, and found that migraine patients responded to cortical activation in a pattern similar to that seen in normal control subjects in response to cortical inhibition. These data were taken to indicate that the occipital cortex of migraine patients is hypo-excitable.

Aurora and colleagues (Aurora, Al-Sayeed, & Welch, 1999; Aurora & Welch, 2000; Aurora, & Welch, 1998; Aurora, Welch, Bhardhwaj, & Ramadan, 1998) reported that migraine patients were significantly more likely to experience phosphenes than healthy control subjects since they had a significantly lower threshold for phosphene generation. These findings were taken to suggest that the visual cortex of patients with migraine is significantly more excitable than that of healthy control subjects and to be consistent with the hypothesis that CSD may be an important part of the underlying mechanism of migraine. TMS data are indicative of a difference in cortical excitability between healthy control subjects and patients diagnosed with migraine, however, the determination of whether the brain is hyper- or hypoexcitable requires further study and/or supporting evidence from other avenues of research, such as neuroimaging.

Neuroimaging Studies

Magnetic resonance imaging (MRI) offers a noninvasive method to study the cerebral nervous system and provides an avenue through which the possibility that cortical spreading depression might be responsible for the pathogenesis of migraine can be investigated. MRI blood oxygen level–dependent investigations have demonstrated that CSD-like phenomena can be detected via neuroimaging methods (Cao, Welch, Aurora, & Vikingstad, 1999; Hadjikhani, Sanchez Del Rio, Wu, Schwartz, et al., 2001).

A functional MRI (fMRI) study that applied stimuli designed to elicit visual discomfort by changing colour illumination reported increased neuronal responses in MA

patients as compared to healthy control subjects (Huang, Cooper, Satana, Kaufman, et al., 2003). Huang et al. (2003) concluded that migraine associates with a higher susceptibility to visual distortions, which predisposes the cortex to spontaneous neuronal depolarization followed by cortical spreading suppression of functioning. The fMRI results of Hadjikhani et al. (2001) showed a slowly spreading area of abnormal blood flow in the occipital lobe during the migraine aura and provide added support to the hypothesis that migraine is not the consequence of cortical ischemia, but the result of the abnormal neuronal firing associated with CSD.

A recent magnetic resonance imaging study reported that a diagnosis of MA was associated with an increased risk of infarct when the number of migraine attacks exceeds one per month (Kruit, van Buchem, Hofman, Bakkers, et al., 2004). Using Dutch population surveys, Kruit and colleagues selected a representative group of migraine patients with- ($n = 161$) and without aura ($n = 134$) and found no significant difference in the prevalence of overall infarct in patients with migraine (8.1%) when compared to healthy control subjects (5.0%; $n = 140$) matched for age (30 to 60 years old), education, and city of residence. The prevalence of infarct in the posterior cerebellar region in the migraine patients (5.4%) was significantly higher that that of the healthy control group (0.7%). When aura symptoms were used to classify the patient group, the prevalence of infarct in patients with MO was 2.2%. This difference was statistically significant from the patients with MA ($p < .05$), but not from the control subjects. Kruit et al. (2004) concluded that frequent migraine attacks increase the risk of deep white matter lesions and hypothesized that migraine patients from the general population are susceptible to

sub-clinical posterior cerebellar infarcts. These authors also suggested that, in some instances, a diagnosis of migraine might lead to progressive brain damage.

Migraine and Psychiatric Factors

Similar to other pain conditions, it is reasonable to assume that a diagnosis of migraine might lead to increased worrying and vulnerability to pain, anxiety, dysphoria, and a higher risk of depression. Hardebo (1991) has suggested that migraine with aura has a negative effect on the autonomic nervous system, specifically the hypothalamus. This brain region is involved in the regulation of behavioral responses associated with survival (e.g., rage, fear reactions), and lesions result in a variety of symptoms including diminished emotional reactivity and changes in mood states. Understanding the nature of the relation between migraine and depression or anxiety could improve our understanding of the etiology of these conditions and influence the choice of treatment. In addition, accounting for symptoms of anxiety and depression could help differentiate cognitive effects associated with migraine from those related to coexisting psychiatric conditions. Several studies have reported increased incidence of anxiety and depressive symptoms in patients diagnosed with migraine (Devlen, 1994; Garvey, Tollefson, & Schaffer, 1984; Jarman, Fernandez, Davies, Glover, et al., 1990). Psychiatric comorbidity in migraine was found to exacerbate the impact of the illness and substantially increase the associated medical expenses. An investigation of the medical costs associated with a diagnosis of depression and anxiety revealed that the total medical costs for outpatients with comorbid migraine were $6,524 versus $1,400.5 for outpatients without migraine, while the costs

for inpatients with comorbid migraine were $2,184.4 versus $559.1 for inpatients without migraine (Pesa & Lage, 2004).

A comparative study of patients with migraine and with chronic daily headache revealed that 24% of the migraine sample reported mild symptoms, 12% moderate symptoms, and 6% moderate-severe symptoms of depression (Magnusson & Becker, 2002). A large-scale epidemiological study of headache conducted in the Detroit area (Breslau, Schultz, Stewart, Lipton, Lucia, & Welch, 2000) reported that migraine (n = 536) and severe headache (n = 162) groups had significantly higher lifetime prevalence rates of depression than normal control subjects (n = 586). These depression rates were 40.7% for migraine, 37% for severe headache, and 16% for the control subjects. In a subsequent investigation by the same group, the risk of developing migraine in people with major depression was three times higher than in those without such a history, and the risk of developing major depression in people with migraine was five times greater than in those without a history of headaches (Breslau, Lipton, Stewart, Schultz, & Welch, 2003). Breslau and colleagues concluded that the relationship between migraine and depression is bidirectional with each disorder increasing the risk of onset of the other. Although the presence of depression does not appear to worsen the course of migraine over time, migraine headaches are more disabling in the presence of major depression. Pharmacological treatments targeting both disorders may be beneficial to patients with comorbid pathology (Breslau et al., 2003; Sheftell & Atlas, 2002).

In an investigation of adult siblings with and without migraine, Persson (1997) found that patients with migraine displayed significantly higher neuroticism or trait anxiety characteristics, were more sensitive, and showed greater signs of anxiety than their migraine-free counterparts. Thus, Persson proposed that psychotherapy should be considered along with medication as an alternative prophylactic treatment for migraine.

Another project, conducted in Sweden, investigated associations between migraine, major depression, panic disorder, and neuroticism in women aged 40 to 74 years old, and reported a strong correlation between active migraine attacks, a history of major depression, high levels of stress susceptibility and somatic trait anxiety in 60-74 years old women cohort (Mattsson & Ekselius, 2002). A similar examination of the long-term association between personality traits, depression, and migraine concluded that even though short-range treatment is not influenced by the co-occurrence of migraine, personality changes, and depression in women this relationship is noteworthy in the long-term (Mongini, Keller, Deregibus, Raviola, et al., 2003).

Migraine and Studies of Cognitive Function

Several investigations have addressed the possibility that subtle cognitive deficits might be associated with migraine. However, despite the substantial burden that migraine places upon society, the number of neuropsychological investigations addressing the possible correlation between diminished cognitive performance and migraine is relatively small. Some reports found no important cognitive differences

between patients diagnosed with migraine and healthy control subjects (Bell, Primeau, Sweet, & Lofland, 1999; Leijdekkers, Passchier, Goudswaard, Menges, & Orlebeke, 1990). Other investigations described deficits on measures of attention, information processing, sensorimotor function, language, and memory (D'Andrea, Nertempi, Milone, Joseph, & Cananzi, 1989; Hooker & Raskin, 1986). As with other methods of investigation, the conflicting cognitive profiles found in migraine may be explained by diverse inclusion criteria and the uneven sensitivity of the neuropsychological measures employed. These factors limit the validity of the conclusions drawn and preclude generalization. A review of studies investigating the association between migraine and cognitive performance ensues, however for ease of presentation; the specific neuropsychological measures used by each study are listed in Appendix A.

Migraine and Normal Cognitive Performance

Despite evidence substantiating cognitive disturbances in migraine patients, data showing no distinction between the cognitive performance of patients with migraine and normal control subjects are also available. Leijdekkers et al. (1990) compared migraine with and without aura to healthy control subjects and reported no cognitive impairment in the migraine groups. Their groups comprised 37 patients (26 patients diagnosed with MO and 11 diagnosed with MA) and 34 healthy control subjects who performed similarly on all cognitive measures employed (Appendix A). No relationship was established between the duration of illness, medication history, and level of cognitive performance. Given that all the measures used in this study were designed to test relatively basic

cognitive abilities, Leijdekkers et al. (1990) acknowledged the possibility that their battery was not capable of detecting high-level differences in cognitive skills between patients diagnosed with migraine and healthy control subjects.

In a different study, Bell et al. (1999) reported no significant association between chronicity and cognitive impairments was present in an investigation comparing the performance of chronic migraine sufferers (n = 20) against that of patients with non-headache chronic pain (n = 20) and mild traumatic brain injury (n = 20). Factor analysis was used to derive three index scores of cognitive efficiency, memory, and visual-perceptual ability (Appendix A). While the migraine and chronic pain groups performed similarly, the mild traumatic brain injury group's performance was significantly below that of the other two groups. Because the migraine group included patients with mixed clinical profiles (i.e., chronic pain not related to migraine, tension-type headaches) significant differences between the migraine and chronic pain groups might have been obscured by the heterogeneous characteristics of the migraine group. Additional analyses focused on performance within each group and patients were determined to meet the criteria for cognitive impairment if their performance on three or more tasks was below the fifth percentile when compared to instrument specific normative data. Based on this definition 5% of the migraine group, 15% of the chronic pain group, and 30% of the traumatic brain injury group were cognitively impaired. A less stringent definition of cognitive impairment required patients to perform below the 16th percentile on five or more of the instruments administered. According to this latter definition 10% of the migraine group, 15% of the chronic pain group, and 40% of the traumatic brain injury

group were impaired. Bell et al. concluded that regardless of the adopted definition for cognitive impairment, only the mild traumatic brain injury group performed significantly poorer than the norm. It should be noted that because a normal control group was not included, the comparison against normative standards might not have adequately captured the presence of cognitive differences between migraine and healthy control subjects. Bell and colleagues reported no significant effects of migraine on cognitive abilities; however, they did not address the possible implications for the 5% of the patients who met the authors' stringent criteria for cognitive deficits.

A pilot study using the Headache Care Center-Automated Neuropsychological Assessment Metrics battery to measure the cognitive abilities of ten patients who had used sumatriptan injection in the past for relief of migraine headaches was carried out by Farmer, Cady, Bleiberg, & Reeves (2001). Baseline testing (Appendix A) was administered during headache-free periods, and repeat tests were administered while the patients experienced an untreated migraine episode and at 15, 30, and 45 min post-injection with sumatriptan. Migraine onset was accompanied by significant decline in cognitive functioning, but the disruption in cognitive performance was reversed following the administration of migraine-specific medication at the 15-minute time interval and continued to improve above baseline at 30 and 45 minutes. The level of cognitive performance of the migraine patients during migraine-free intervals was not compared against that of non-migraine control subjects and it is unclear whether the improvement in cognitive performance could be attributed solely to medication. Given that performance at the 30 and 45-minute intervals improved beyond baseline levels, one

might suspect that familiarity with testing might have lead to artificially higher levels of performance.

In another evaluation of cognitive functions of chronic migraine sufferers with- and without aura, patients with cluster headaches, and healthy control subjects, Sinforiani and colleagues reported no significant differences between patients and control subjects on any of the neuropsychological (Appendix A) and tachistoscopic tasks administered (Sinforiani, Farina, Mancuso, Manzoni, Bono, & Mazzucchi, 1987). Results were analyzed with one-way ANOVA and t-tests and it was concluded that there was no indication of cortical dysfunction in migraine.

Jelic, van Boxtel, Houx, & Jolles (2000) conducted a study using data from a large population-based sample (n = 1869) and reported that although age had a large effect on processing speed and memory, the presence of a diagnosis of migraine did not influence cognitive performance (Appendix A). Their subject sample was divided into patients with migraine (n = 99; 65 women, 34 men) and headache-free control subjects (n = 1768). The lack of significant interactions between age and migraine with regard to processing speed and memory lead the authors to conclude that migraine diagnosis does not affect cognitive functioning in the young, middle-aged, or older adults compared to the general population. It is unclear, however, whether the patient population used in this study was given a diagnosis of migraine in accordance with the International Headache Society guidelines.

A study investigating the impact of medication on the ability of migraine patients to resume their normal level of functioning showed that groups of MA (n = 17), MO (n = 48), chronic daily headache (n = 5), and cluster headaches (n = 7) patients presented significant cognitive decline during headache attacks (Meyer, Thornby, Crawford, & Rauch, 2000; Appendix A). Performance was, however, found to return to normal levels following sleep or treatment with serotonin agonists. The depression symptoms remained unchanged during visits with or without concurrent headaches. Meyer et al. concluded that any recorded cognitive impairments associated with headaches are temporary and might be the result of abnormal serotonin release.

Palmer & Chronicle administered three separate cognitive tasks to patients diagnosed with MA (n = 12) and without aura (n = 12), and a group of healthy control subjects (n = 12). All the tasks were computer administered and employed a divided model in which stimuli were presented equally often in either visual field. No differences on reaction time or accuracy of response were observed between the groups on any of the tasks administered (Appendix A). The authors concluded that the direct application of speeded reaction time tasks might not be useful to the study of cortical hyperexcitability in migraine.

Migraine and Diminished Cognitive Performance

D'Andrea et al. (1989) employed personality and cognitive instruments to evaluate twenty children diagnosed with migraine headaches without aura (Appendix A).

Children diagnosed with migraine showed significantly higher levels of anxiety than a sample of normal control children and exhibited an increased ability to inhibit aggressive responses on a Picture Frustration Test, and the authors concluded that migraine without aura is associated with minor psychological abnormalities that are likely to manifest themselves under stressful circumstances. Evaluation of cognitive abilities indicated that healthy control children outperformed those diagnosed with migraine on measures of verbal and non-verbal memory. D'Andrea et al. (1989) proposed that diminished memory skills might account for school performance differences between children with migraine and their healthy counterparts.

A study of the cognitive performance of patients with severe migraine (n= 19) revealed that they obtained consistently lower scores on memory and information-processing tests than their matched normal control (n = 19) counterparts (Zeitlin & Oddy, 1984; Appendix A). According to Zeitlin & Oddy, the cognitive differences could not be explained by the presence of higher anxiety, obsession, and somatic symptomatology in the patients over that seen in the normal control subjects.

In a subsequent investigation, Hooker & Raskin (1986) administered an extensive neuropsychological battery to migraine patients with aura (n = 16), migraine patients without aura (n = 15), and headache-free subjects (n = 15; Appendix A). Raw scores were coded on a six-point scale with zero indicating high normal performance and five indicating severe impairment and data were combined into two cognitive indices. An 'Average Impairment Index' was derived as the mean of coded raw scores and a

'Percentile Impairment Index' was taken as the percent of tests with scaled scores in the impaired range, as defined by these authors. Both migraine groups obtained significantly lower scores than the control group on a finger-tapping task, a complex motor discrimination task, and in the delayed recall of prose passages. Migraine with aura patients obtained significantly lower scores than the migraine without aura patients and control subjects on the Digit Symbol subtest of WAIS-R, the Purdue Pegboard test and the Aphasia Screening Test. Hooker & Raskin (1986) argued that the pattern of results observed in their migraine patient groups is consistent with a disorder of the central nervous system in which MA is associated with more sizeable functional decrements than MO.

Waldie, Hausmann, Milne, & Poulton (2002) investigated the association between migraine and cognitive ability among the members of a longitudinal birth cohort study and tested these subjects when they were 3, 7, 9, 11, 13, and 26 years old (Appendix A). At age 26, several of their subjects were diagnosed with migraine and tension headache. Statistical analyses of the longitudinal data revealed that patients with migraine performed poorer than those diagnosed with tension-type headaches and headache-free individuals on Verbal IQ ratings and verbal comprehension measures given at 3, 7, 9, 11, and 13 years old. Patients with migraine performed significantly poorer than patients with tension-type headaches and the normal control subjects on verbal abstract reasoning (similarities subscale) at testing ages 7 to 13. In addition, their scores were significantly worse than those of normal control subjects in general and word knowledge (information and vocabulary subtests). Separate analyses showed that subjects with childhood

headaches were outperformed by those without a history of headaches on Verbal IQ, but this effect was restricted to those individuals who were later diagnosed with tension-type headaches and those for whom headaches did not persist. Migraine patients with childhood headaches performed similarly to normal controls subjects at all assessment ages. Waldie et al. (2002) advanced the notion that the relation between migraine and verbal impairment is one of shared risk factors, but not of causality because the verbal impairment was unrelated to the length of headache history, medication use, or the severity and duration of the migraine attacks. Alternatively, they hypothesized that a generalized impairment in selective attention in the migraine group could lead to diminished verbal performance.

Using a reaction time paradigm, Wray, Mijovic-Prelec, & Kosslyn (1995) reported that patients with MA displayed a reaction-time advantage on simple, but not complex visual detection tasks. Their subject groups included 12 patients diagnosed with MA (10 females and two males) and 12 gender-matched healthy control volunteers. Testing was conducted using four computer generated visual paradigms designed to test low-level and high-level visual processing (Appendix A). The migraine patients demonstrated superior ability to detect and process low-level visual stimuli but lost this advantage when high-level visual processing was required. Wray et al. interpreted these results as suggesting a selective damage of the inhibitory circuit of the primary visual cortex in migraine or perhaps as suggesting that the migraine brain might be more excitable than that of healthy control subjects.

Conlon & Humphreys (2000) failed to reproduce the processing speed advantage found in the MA group by Wray et al. (1995). However, they showed that patients with high scores on a visual discomfort task performed significantly slower on tests of automatic and conscious attention (Appendix A). The study groups included MA patients, MO patients, patients with non-specific headaches, and headache-free normal control subjects. Conlon & Humphreys proposed that the significant difficulties present in the high-visual discomfort migraine group could be explained by increased sensory sensitivity or diminished spatial attention focus leading to slower search times.

The possibility that cognitive decreases associated with migraine might be related to the chronicity of the disease was investigated in 60 patients with migraine (Calandre, Bembibre, Arnedo, & Becerra 2002). Groups were classified according to the presence (n = 10) and absence (n = 50) of aura symptoms. Significant differences were noted only on a reaction time task on which all patients were significantly slower than the normal control subjects. Subdividing the patient group according to the length of headache history into those with a diagnosis of over and under 20 years, showed reductions in verbal and non-verbal memory, attention, and visuo-motor speed processing among patients with a longer history of migraine and elevated attack frequency (Appendix A). Patients and control subjects presented similar levels of depressive symptoms. The higher levels of anxiety present in the migraine patients with frequent attacks were not correlated with the cognitive results, suggesting that their cognitive performance was not modulated by emotional factors. Similar to Zeitlin & Oddy (1984), these data were taken to suggest that migraine patients present cognitive decreases when compared to normal

control subjects and these significant differences cannot be attributed to coexisting psychiatric symptomatology.

Mulder, Linssen, Passchier, Orlebeke, de Geus (1999) found that patients diagnosed with MA (n = 10) showed motor slowing and delayed responses on tasks involving sustained and selective attention processes when compared to a group of patients with MO (n = 20) and normal control subjects (n = 30). Testing consisted of the Neurobehavioural Evaluation System, Second Edition designed to examine a broad spectrum of cognitive abilities (Appendix A). Principal component analysis was used to reduce data into five cognitive domains: reasoning, reaction speed, selective attention, digit encoding, and pattern perception. Overall, patients with migraine and normal control subjects differed only on the pattern memory component of the pattern perception domain, with the patient group performing significantly slower. Comparisons between the migraine with and without aura revealed that the patients with aura were significantly slower on the finger-tapping task, symbol substitution, and on all tasks pertaining to the selective attention domain. The normal control subjects and the patients with migraine without aura performed similarly on these tests. The cognitive deficits were not aggravated by preceding migraine attacks, use of medication, or attack length. Because prefrontal activation has been associated with selective and sustained focusing of attention on tasks such as the Stroop, Mulder et al. (1999) hypothesized that the attention deficits present in the migraine patients with aura might reflect a functional disturbance in the prefrontal cortex.

Psychomotor dysfunction in migraine patients was also reported by Scherer, Bauer, & Baum (1997). Patients diagnosed with migraine (n = 25) were compared to a group of patients diagnosed with multiple sclerosis (n = 22) and a healthy control subject group (n = 41) on an alternate finger-tapping test. Only in the less than 40 years-old subgroups, female migraine patients and male and female patients with multiple sclerosis were significantly slower in their performance than the normal control subjects. Given that the finger-tapping test is thought to be sensitive to minimal white matter dysfunction, Scherer et al. (1997) proposed that a significant portion of migraine patients younger than 40 years (46% of the sample investigated) might present slight structural abnormalities in the white matter of the brain.

Le Pira and colleagues investigated the cognitive abilities of migraine patients with and without aura (Le Pira, Zappala, Giuffrida, Lo Bartolo, Reggio, Morana, & Lanaia, 2000). The two groups of patients performed similarly and the duration of their illness was not correlated with any recorded diminished cognitive abilities (Appendix A). Migraine patients with and without aura performed poorly in the immediate and delayed recall of the Rey complex geometric figure. Patients with migraine without aura performed significantly worse than the normal control subjects on a verbal memory task as well as on a task associated with attention abilities. The authors argued that the presence of memory difficulties seen in the migraine patients were the result of a defective learning strategy leading to impaired recall abilities. The low scores on visual and attention tasks along with the visuo-spatial processing difficulties found in the migraine group were attributed to possible right hemisphere dysfunction.

McKendrick & Badcock (2004) investigated the possibility that visual processing abnormalities might be present in individuals with migraine. A frequency-doubling perimetry task was used to assess pre-cortical visual function and a motion-coherence perimetry task evaluated cortical visual processing. A minority of patients diagnosed with migraine showed localized visual field deficits as compared to normal control subjects, but these differences failed to reach significance at the group level. In contrast, the majority of migraine patients performed poorly on a task associated with global visual processing of motion. Fifteen of the patients with MA (n = 19) and eleven of the patients with MO (n = 17) demonstrated decreased ability to detect coherent motion. Of the 21 healthy control subjects, only one subject could be classified as meeting the criteria for motion coherence abnormality. McKendrick & Badcock suggested that although a deficiency of habituation could be a plausible explanation of cortical visual abnormality, the repetitive stimuli used in their investigation were not presented in the same location in succession, thus rendering habituation an unlikely mechanism. Instead, they argued that the poor performance exhibited by the migraine patients, regardless of the presence or absence of aura symptoms, might be explained by increases in baseline neuronal noise, consistent with the hypothesis of cortical hyperexcitability.

In a follow-up investigation applying an identical test battery to that reported in the 2000 study, Le Pira and colleagues explored the impact of the unilaterality of migraine on verbal and non-verbal cognitive abilities (Le Pira, Lanaia, Zappala, Morana, Panetta, Reggio, & Reggio, 2004). Two groups of migraine patients with and without

auras were divided according to the laterality of the headache pain and the attack frequency was used as a separate grouping factor. The use of prophylactic and antidepressant medication was not considered exclusionary, and a separate healthy control group was not included. Although attack frequency was not associated with performance differences, migraine patients with right-sided pain with or without aura obtained substandard results on the Rey Complex Figure and produced fewer semantic clusters on the second trial of California Verbal Learning Test. Le Pira et al. (2004) hypothesized that the weak cognitive performances in patients with right-hemisphere migraine are the result of right-hemisphere dysfunction.

The available evidence regarding the cognitive profiles of migraine patients remains mixed and provides a clear indication that additional data are needed to clarify the impact of migraine on general cognitive functioning. Several researchers reported no correlation between migraine and cognitive difficulties (Bell et al., 1999; Jelic et al., 2000; Leijdekkers et al., 1990; Sinforiani et al., 1987). Others, however, found that migraine was associated with lower cognitive and motor performance (Calandre et al., 2002; Conlon & Humphreys, 2000; Hooker & Raskin, 1986; Le Pira et al., 2004; McKendrick & Badcock, 2004; Mulder et al., 1999; Scherer et al., 1997; Waldie et al., 2002; Wray et al., 1995; Zeitlin & Oddy, 1984). The majority of the research reporting a negative impact of migraine on cognitive skills suggests that this neurological disorder is associated with difficulties, especially in the areas of attention, verbal and visuo-spatial memory, and motor performance.

Hemispheric Lateralization of Cognitive Functions

Previous observations from patients with unilateral brain lesions have generated a large body of evidence solidly in favor of hemispheric specialization of psychological processes. In right-handed individuals, damage to the left frontal and left temporal lobes was shown to be frequently associated with speech impairments and the left hemisphere is therefore known to be dominant for speech (Milner, 1971). In left-handed people, the association between language and hemispheric localization is less clear since right-hemisphere language dominance has been demonstrated in a significant percentage of left-handed neurological patients (Loring, Meador, Lee, Murro, Smith, Flanigin, Gallagher, & King, 1990; Rasmussen & Milner, 1977; Vargha-Khadem, O'Gorman, & Watters, 1985; Woods, Dodrill, & Ojemann, 1988). Specialized tests have been developed to determine the hemispheric side of language lateralization and the unilateral intracrotid injection of sodium amobarbitol has become one of the most routine pre-surgical procedures used (Wada & Rasmussen, 1960). Rasmussen & Milner (1977) used this test to examine the effect of brain injury and hand preference on language lateralization in 396 epilepsy patients and reported that approximately 96% of right-handers and 70% of left-handers showed left hemisphere dominance for simple speech functions when there was no clinical evidence of early damage to the left hemisphere. Other sodium amobarbitol studies have reported left-hemisphere dominance for language in 63% to 96% of right-handers, and 48% to 75% of left-handed and ambidextrous patients (Branch, Milner, & Rasmussen, 1964; Helmstaedter, Kurthen, Linke, & Elger, 1997; Loring et al., 1990; Mateer & Dodrill, 1983; Rausch & Walsh, 1984; Risse, Gates,

& Fangman, 1997; Strauss and Wada, 1983; Woods et al., 1988; Zatorre, 1989). Although useful for the study of language laterality, the sodium amobarbitol procedure is not performed in normal control subjects because of its invasive nature and the associated health risks. Recent approaches have applied a functional transcranial Doppler sonography to investigate hemispheric language dominance in healthy control subjects. Knecht, Dräger, Deppe, Bobe, et al. (2000) used this technique in 326 healthy subjects and, similar to Rasmussen & Milner's 1977 study, they found that the incidence of right-hemisphere language dominance was strongly associated with left-hand preference such that it was present in only 4% of right-handers, 15% of ambidextrous subjects, and 27% of left-handers. Other studies using functional magnetic resonance imaging and repetitive transcranial magnetic stimulation reported that left-hand preference correlated with right-hemisphere language activation in 8% to 10.5% of their subjects (Khedr, Hamed, Said, & Basahi, 2002; Pujol, Deus, Losilla, & Capdevila, 1999; Szaflarski, Binder, Possing, McKiernan, et al., 2002). In addition to language, the left hemisphere is also dominant for the recall of verbal information and significant verbal memory impairments have been demonstrated in left hemisphere lesions involving the temporal lobe (Milner, Squire, & Kandel, 1998; Squire & Zola, 1998; Trenerry & Loring, 1995; Zola-Morgan & Squire, 1993).

The right hemisphere has been known as the "minor hemisphere" and is typically responsible for tasks involving visualization of spatial relations (Bogen, 1969; Gazzaniga, Bogen, & Sperry, 1965; Kolb & Whishaw, 2003; Milner & Taylor, 1972). The right posterior cortex has been originally associated with visuospatial perception by Jackson

(1864). Damage to the right parietal cortex was shown to induce severe contralateral neglect; deficits in visual search, in topographical and in spatial localization; (Damasio, Tranel, & Rizzo, 2000; Farah, 2003; Heilman, Watson, & Valenstein, 2003; Mesulam, 1985; Rafal, 1997). The right-parietal syndrome is associated with impaired perception of social or emotional signals, as well as anosagnosia, the inability to recognize the presence of difficulties (Adair, Schwartz, & Barrett, 2003; Code, 1987; Heilman et al., 2003; Ross, 2000; Segalowitz, 1983).

The available evidence regarding the impact of migraine hemispheric laterality on cognitive abilities is limited to the study of Le Pira and colleagues who, in 2004, reported that migraine is associated with a right hemisphere disadvantage. This investigation will address the need for additional data to determine the impact of left and right migraine laterality on neuropsychological function.

Present Investigation

(1) There is strong evidence suggesting that migraine can be associated with changes in personality, however, these have not been thoroughly studied. Migraine with aura is a more profound neurological illness, and therefore we predict that negative personality traits will be most apparent for this group. In addition, the effects of unilateral hemispheric migraine have not been studied and therefore we will use the NEO-PI personality inventory to determine whether hemispheric lateralization is associated with differences in the personality profiles of left versus right hemisphere

migraine. Previous findings support a left-hemisphere dysfunction in patients with anxiety and social phobia (Bruder et al., 2004; Heller et al., 1995; Keller et al., 2000; Liotti et al., 1991). Consequently, we expect that interference with the normal processing of verbal input in the left hemisphere could lead to the development of negative personality traits in left hemisphere migraine.

(2) Previous research has been equivocal in demonstrating the presence of cognitive differences between patients with migraine and healthy control subjects and between migraine with aura and migraine without aura (Bauer, Evers, Lindörfer, Schuierer, et al., 1997; Hoker & Raskin, 1986; Mulder et al., 1999). In this study we employ a carefully selected group of neuropsychological measures that are sensitive to a wide range of cognitive functions including verbal and visuo-spatial memory, executive and problem solving abilities, and motor skill and we compare the results of the migraine patients to those of a well matched control group.

(3) In this study, we employed rigid selection criteria to choose groups of patients who had a specifically unilateral left or right hemisphere migraine focus. Given the putative negative effects of migraine, we predict that patients with unilateral disease will display difficulties that are consistent with either left or right hemisphere function. Therefore, patients with left-sided migraine should have difficulty with language tasks and the ability to retain verbal information, whereas patients with right-sided migraine should be worse on tasks that rely on the manipulation and encoding of visuo-spatial information.

METHOD

Subjects

The attempt to elucidate the relationship between migraine and cognition is often limited by: 1) patient inclusion criteria; 2) sensitivity of the measures employed to assess cognitive differences; and 3) appropriateness the of selected control group. The present study applied careful selection criteria; used well-standardized neuropsychological measures with demonstrated sensitivity to overall cognitive abilities as well as to left and to right hemisphere function, and recruited a group of healthy control subjects matched to the migraine patients on the demographic characteristics of age, handedness, and years of education.

Patient Inclusion Criteria

A total of 35 right and left-handed patients (32 females, 3males; Mean Age = 41, SD = 13) diagnosed with hemicranial migraine with- and without aura were tested. To eliminate the possibility of differential cognitive abilities associated with left-hand preference, only right-handed patients were included in the statistical analyses (n = 29; 26 females, 3 males; Mean Age = 43, SD = 11). Patients were recruited at the Montreal Neurological Hospital by either one of two neurologists with extensive clinical experience in treating patients with migraine (Dr. Michel Aubé and Dr. Liam Durcan; Appendix B). Diagnosis was based on the 1988 classification of migraine with and

without aura published by the Headache Classification Committee of the International Headache Society (IHS). Appendix C contains copies of English and French Versions of the Consent Forms signed by each study participant, and Appendix D includes contact and confirmation of participation in the study for the patient population.

The patient sample was subdivided as follows: (1) the migraine 'Type' category; (2) the migraine 'Hemisphere' category; and (3) the migraine 'Group' category. The migraine 'type' category includes 12 patients diagnosed with migraine with aura (MA) and 17 patients diagnosed with migraine without aura (MO). The migraine 'hemisphere' category includes 12 patients with left-hemicranial (M_{Left}) migraine, and 17 patients with right-hemicranial (M_{Right}) migraine. Finally, the migraine 'group' category takes into account the hemispheric lateralization of migraine and the presence of aura symptoms, and further divides patients into one of four subgroups: left-hemicranial migraine without aura (n = 7), right-hemicranial migraine without aura (n = 10), left-hemicranial migraine with aura (n = 5), and right-hemicranial migraine with aura (n = 7). Table 1 and Table 2 describe the headache characteristics of these groups and provide a summary of their associated headache features.

Table 1

Descriptive characteristics of the migraine patient sample

Headache features	Mean	SD
Headache history (yrs)	21	14.17
Attack frequency per month	4	2.04
Attack duration (hrs)	32	27.92

Table 2

Associated headache features

Associated features	Percent Present
Nausea	96 %
Photophobia	96 %
Phonophobia	96 %
Other Symptoms (e.g., sensory experiences; weakness on one side of the body)	73 %
Family History of Migraine	80 %

Patient Exclusion Criteria

To eliminate the possibility of artificially inflating any differences between normal control subjects and migraine patients, the presence of current or past medical and/or psychiatric diagnoses was exclusionary. Because patients diagnosed with depression have been shown to obtain lower scores on some cognitive measures as compared to normal control subjects, the migraine patients participating in this study had no reported history of depression. Patients were screened for systemic and/or CNS disease (e.g., epilepsy, head injury); history of learning disability; history of psychiatric illness (e.g., major depression, generalized anxiety disorder); family history of epilepsy; and menstrual migraine. Pre-selection screening was based on the information present in the medical files and patients failing to meet study inclusion criteria were not contacted for participation. Sixty patients were excluded because of previous or concurrent diagnoses of anxiety, depression, and epilepsy. Additional exclusion criteria for the patient group included current or past (less than 6 months) history of substance abuse (e.g., opiate analgesics, psychotropic drugs, over 10 mg/week of ergotamine, over 315 g/week alcohol). Patients were not prescribed prophylactic medication at the time of recruitment; however, most used symptomatic medication including triptans and/or Non Steroidal Anti-Inflammatory drugs (NSAID) to control their headaches.

Normal Control Subject Inclusion Criteria

The healthy control subjects did not experience migraine headaches and were in good mental and physical health. A group of 12 healthy control subjects (8 females, 4 males; Mean Age = 37.5, SD = 13.4) was matched to patients diagnosed with migraine on age, handedness, and years of education. The final group of normal control subjects included 10 right-handed individuals (6 females, 4 males; Mean Age = 37, SD = 13).

Emotional State

The participants' affective state was evaluated using the Beck Depression Inventory and the State Trait Anxiety Inventory (Appendix E and Appendix F). Both inventories were administered to confirm that the emotional state of the patient and control groups was comparable at the time of the administration of the neuropsychological measures.

Beck Depression Inventory

The Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, et al., 1961) is a 21-item test presented in multiple-choice format designed to measure the presence and degree of depression in adolescents and adults. The items of the BDI assess specific symptoms or attitudes that are thought to characterize depressed patients, and are consistent with descriptions of depression contained in the psychiatric literature. Each

item is assigned a numerical value of zero, one, two, or three to indicate degree of severity. A maximum score of 63 can be obtained. Score cut-off guidelines are: 1) score less than 13 associated with no evidence of depression; 2) score of 14-19 associated with mild depression; 3) score of 20-29 associated with moderate depression; and 4) score above 30 associated with severe depression. For this investigation, scores equal to or greater than 19 would be considered exclusionary.

State Trait Anxiety Inventory

The State Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, & Lushene, 1970) has two 20-item scales that provide a measure of anxiety in adults. It is designed to differentiate between the temporary condition of state anxiety and the more general and long-standing quality of trait anxiety. Each subscale has 20 questions with a range of 4 possible responses to each (i.e., 1 = Almost Never; 2 = Sometimes; 3 = Often; 4 = Almost Always). The essential qualities evaluated by the STAI State-Anxiety scale are feelings of apprehension, tension, nervousness, and worry. Scores on the State scale increase in response to physical danger and psychological stress, and decrease with relaxation training. On the STAI Trait-Anxiety scale, consistent with the trait anxiety construct, psychoneurotic and depressed patients generally have high scores.

Personality

NEO Personality Inventory

The NEO Personality Inventory (NEO-PI; Costa & McCrae, 1985) was administered to investigate potential personality differences between normal control subjects and migraine patients. This inventory provides scores for five personality factors that are based on research using personality questionnaires and factor analysis. The five factors are 1) Neuroticism; 2) Extraversion; 3) Openness to Experience; 4) Agreeableness; and 5) Conscientiousness. High scores on Neuroticism are associated with increased levels of anxiety, angry hostility, depression, self-consciousness, impulsiveness, and vulnerability, while low scores are associated with calm, even-tempered, relaxed, composed, and confident personalities. High scores on Extraversion correlate with warm, gregarious, assertive, active, excitement seeking, upbeat, and energetic personalities, while low scores are characteristic of reserved, independent, even-paced, less exuberant, serious personalities. High scores on the Openness to Experience scale correlate to intellectually curious individuals with an active imagination, artistic spirit, increased attention to inner feelings, and a preference for variety of experience. Low scores on this subscale are associated with individuals with a narrower scope of interests, who apply conventional thought processes, are conservative and cautious in their approaches. High scores on the Agreeableness factor are characteristic of trusting, straightforward, altruistic, compliant, modest, tender-minded, and cooperative individuals. Low scores on this factor are associated with skeptical, egocentric, competitive, headstrong personalities. High scores on the Conscientiousness

scale are associated with competent, organized, achievement oriented, self-disciplined individuals while low scores are traits of easy-going, sometimes careless, spontaneous, absent-minded, and distractible individuals.

Neuropsychological Test Battery

An extensive neuropsychological battery was administered and the instruments were selected based on previously demonstrated sensitivity to the function of either cerebral hemisphere (Table 3). The test battery was individually administrated in a fixed order and had a mean duration of 3½ hours (Appendix G). Patients with migraine were tested during migraine-free periods. Appendices H through P provide example forms/illustrations of the French translations for the instruments administered in this study. Groups were evenly divided between English and French speaking participants (normal control subjects: 4 French and 6 English; left-hemicranial migraine without aura: 4 French and 3 English, right-hemicranial migraine without aura: 5 French and 5 English, left-hemicranial migraine with aura: 3 French and 2 English, and right-hemicranial migraine with aura: 3 French and 4 English).

Table 3

Neuropsychological test battery

Behavioural Instrument	Measured Ability	Putative Brain Regions
Handedness Questionnaire	Hand preference	
WASI[1]	General intellectual function	
Verbal IQ	Verbal cognitive abilities	Left hemisphere
Performance IQ	Visuo-spatial cognitive abilities	Right hemisphere
WMS–III[2]		
Faces	Memory for unfamiliar faces	Right medial occipito-temporal
Letter-Number Sequences	Working memory	Bilateral orbito-frontal; dorsolateral prefrontal; posterior parietal
Digit Span	Attention; working memory	Left temporal
CVLT–II[3]	Verbal learning and memory	Left temporal
WMS–R Logical Memory Passages	Immediate and delayed recall for verbal memory	Left temporal
Rey Complex Figure	Visuospatial constructional ability; visuospatial memory	Right temporal
Word Fluency	Time-constrained spontaneous word production	Left inferior frontal gyrus
Stroop Test	Attention; inhibition/mental flexibility; processing speed	Left and possibly right prefrontal cortex
Tapping Test	Motor speed and coordination	Primary motor and premotor
Grooved Pegboard Test	Finger and hand dexterity	Primary motor and premotor
Pinch Strength Test	Finger Strength	Primary motor and premotor
CANTAB[4]		
Spatial Span	Simple visuospatial attention	Right ventrolateral prefrontal cortex
Spatial Working Memory	Visuospatial working memory; search strategy	Dorsal and ventral prefrontal regions, bilaterally
Visual Paired Associates Learning	Ability to form visuospatial associations	Right temporal
Rapid Visual Information Processing	Visuospatial and sustained attention	Dorsal and ventral prefrontal regions, bilaterally
Match to Sample Visual Search	Visual discrimination; reaction time	Primary motor and premotor
Intradimensional/ Extradimensional Set-Shifting	Rule learning; attentional set-shifting	Dorsolateral prefrontal cortex; orbitofrontal cortex
Stockings of Cambridge	Visuospatial planning	Parietal and dorsolateral frontal cortex, bilaterally; left caudate; basal ganglia

Note. [1]WASI = Wechsler Abbreviated Scale of Intelligence; [2]WMS = Wechsler Memory Scale; [3]CVLT = California Verbal Learning Test; [4]CANTAB = Cambridge Neuropsychological Test Automated Battery.

Handedness Questionnaire

The Handedness Questionnaire was used to determine hand preference (Oldfield, 1971). The test includes 18 questions scored on a 5-point scale. Subjects are classified as right-handed if they obtain a score of less than 30, mixed-handed if they score 30-54, and left-handed if they score above 54 (Appendix H). Results on this questionnaire were used to determine final inclusion; patients with scores of 30 or more were not included.

Wechsler Abbreviated Scale of Intelligence (WASI)

The WASI is an individually administered instrument with four subtests that are strongly associated with general cognitive abilities that was normed for an extensive sample of 6 to 89 years olds (Wechsler, 1999). It provides scores for four subscales which are used to calculate Verbal IQ (Similarities and Vocabulary), Performance IQ (Block Design and Matrix Reasoning), and a Full Scale IQ rating.

The Similarities subtest is a test of verbal concept formation, abstract verbal reasoning ability, and general intellectual ability that requires one to explain the similarities of each of 26-paired items (e.g., how are bus and car alike?). Abstract responses receive more credit than concrete responses. Scores on the Similarities subscale represent one of the best indicators of left hemisphere function of the Wechsler Scales of Intelligence subtests, and has been shown that patients with lesions in the left frontal lobe have significantly lower scores than those with lesions in the corresponding

right anterior brain regions (Rzechorzek, 1979; Warrington, James, & Maciejewski, 1986).

The Vocabulary subtest reflects social, economic, and cultural knowledge and consists of 42 words defined by the test taking individual. This subtest explores the degree of verbal knowledge, expressive vocabulary, crystallized and general intelligence, memory, learning ability, and language development and is most sensitive to left hemisphere function. On positron emission tomography, performance on the Vocabulary subtest has been associated with increased glucose metabolism in the left- as compared to the right-temporal lobe and is often found to be sensitive to left hemisphere lesions (Chase, Fedio, Foster, Brooks, et al., 1984; Parsons, Vega, & Burn, 1969).

The Block Design subtest requires assembly of 13 designs presented in order of difficulty. Two-dimensional patterns are produced using either four or nine three-dimensional blocks. This subtest relies on adequate visuospatial abilities, good motor execution, and produces a measure of visuo-spatial construction. Studies of constructional apraxia, defined as an inability to draw freely or copy designs and to build or assemble things, report that performance on this subtest is most strongly affected by right hemisphere lesions especially in the posterior parietal areas (Black & Strub, 1976; Newcombe, 1969; Reitan, 1986).

The Matrix Reasoning subtest provides a measure of nonverbal fluid abilities. Subjects complete 35 abstract patterns by indicating the correct missing portion of the pattern from five possible choices. The Matrix Reasoning subtest was designed to assess

problem-solving skills. Some studies using this subtest to differentiate patients with moderate to severe traumatic brain injury from matched healthy control participants report a lack of sensitivity (Donders, Tulsky, & Zhu, 2001; Martin, Donders, & Thompson, 2000). However, a recent study of patients with stroke, traumatic brain injury, and dementia found the WASI Matrix Reasoning subtest to be sensitive to the cognitive sequelae of both stroke and dementia (Ryan, Carruthers, Miller, Souheaver, et al., 2005).

Wechsler Memory Scale, Third Edition (WMS – III) Subtests

The WMS–III was designed to assess learning, memory, and working memory for individuals in the age range of 16-89 years (Wechsler, 1997). It provides subtest and composite scores that assess memory and attention functions using both auditory and visual stimuli. The Faces, Letter-Number Sequencing, and Digit Span subtests were used in the current investigation.

The Faces subtest requires subjects to retain a series of 24 unfamiliar faces presented for approximately two seconds each, and subsequently recognize these faces when presented along with 24 new unfamiliar faces. Functional imaging has revealed a focal region in the right fusiform gyrus activated specifically during face perception (Kanwisher, McDermott, & Chun, 1997). Prosopagnosia, the inability to process and encode faces, is associated with medial occipitotemporal lesions, especially on the right.

The Letter-Number Sequencing subtest samples sequential processing by requiring an individual to place letters and numbers presented orally in correct order, and provides a measure of auditory working memory abilities. Recent advances in neuroimaging have enabled researchers to establish relatively specific areas of the brain that are involved in working memory. In a positron emission tomography (PET) study, Haut and colleagues examined the pattern of neural activation associated with performance on number-letter sequencing and observed bilateral areas of activation in the orbital frontal lobe, dorsolateral prefrontal cortex, and posterior parietal cortex (Haut, Kuwabara, Leach, & Arias, 2000). Other activation peaks were observed in the right hemisphere, suggesting that participants applied visualization of the verbal information to complete the task.

The Digit Span subtest involves the presentation of sequences of random numbers that increase in length by one digit on subsequent trials until the subject fails two sequences of the same length in a row. The longest sequence successfully completed is the subject's "digit span." Each sequence is read aloud at the rate of one number per second. The individual repeats the sequences of digits either in the same order of presentation or backwards. Digits Forward measures attention and auditory memory while Digits Backward measures active and working memory. Performance fluctuations can suggest problems with attention, concentration, sequencing, number facility, and auditory short-term memory. Hale, Hoeppner, & Fiorello (2002) investigated the association between attention processes and the Digit Span subtest of the Wechsler Intelligence Scale for Children-Third Edition (WISC-III) in 195 children, and concluded

that Digit Backward was associated with attention and executive function processes, while Digit Forward was correlated with short-term auditory memory and therefore left temporal function.

California Verbal Learning Test, Second Edition (CVLT – II)

CVLT-II assesses the strategies and processes used in learning and recalling verbal material (Delis, Kramer, Kaplan, & Ober, 2000). It provides information regarding the subject' short- and long-delay free recall capacities, as well as short- and long-delay cued recall abilities. The subject is required to recall two lists of words that have been read aloud by the examiner. List A is presented five times, while list B is presented one time. Cued recall is assessed by providing the subject with word categories such as "Tell me all the words of the first list that are animals" (Appendix I). Data from patients with left-temporal lobe seizures demonstrated that they are impaired in their ability to learn and recall words; show diminished semantic clustering, and poorer retrieval than either patients with right-temporal lobe seizures or normal control subjects (Hermann, Wyler, Richey, & Rea, 1987). Results from patients with focal frontal- and non-frontal lesions demonstrated that immediate free recall was impaired primarily in patients with posterior left dorsolateral frontal lesions, but also in those with posterior medial frontal lesions, usually bilateral, involving the septal region, and to a lesser degree in those with posterior right dorsolateral frontal lesions (Alexander, Stuss, & Fansabedian, 2003).

Wechsler Memory Scale (WMS)

The WMS Logical Memory Passages (LMP) subtest assesses immediate and delayed verbal logical memory and recall ability (Wechsler & Stone, 1973). This subtest requires subjects to remember two paragraph-length passages that have been read aloud by the examiner (Appendix J). Performance on the LMP subtest by patients with left temporal seizure foci were found to be significantly more impaired than those of patients with right seizure foci (Sass, Sass, Westerveld, Lencz, et al., 1992). Additional support for an intact left hemisphere association with performance on the LMP subtest is available from imaging studies. Manes and colleagues conducted a PET study of the association between blood flow changes in the insular cortex and verbal memory and showed that patients with left insular lesions had poorer immediate and delayed verbal memory as measured by the LMP subtest (Manes, Springer, Jorge, & Robinson, 1999).

Rey Complex Figure

The Rey Complex Figure Test (RCFT) examines visuospatial constructional ability and visuospatial memory using the "complex figure" originally designed by Rey (Rey, 1941; Osterrieth, 1944). It consists of three separate tasks: 1) Copy trial during which one has to copy the complex figure onto a blank sheet of paper while the figure stimulus card remains in plain sight; 2) Immediate Recall requires the subject to draw the figure from memory after the stimulus card has been removed; and 3) Delayed Recall requires the subject to draw the figure from memory 30 to 40 minutes after the Copy trial. The test is scored using specific criteria developed for scoring the accuracy and

placement of individual units of the complex figure. Recall performance on the RCFT by stroke patients with left or right hemisphere damage showed that, when compared to left hemisphere stroke, patients with right hemisphere stroke employed poorer organizational strategy as reflected by low copy accuracy scores and total immediate and delayed recall results (Lange, Waked, Kirshblum, & DeLuca, 2000). Because the memory performance relative to the original amount of visual information encoded did not differ between groups, Lange et al. hypothesized that visuospatial impairment after stroke may be caused by a lack of organizational strategy rather than by a memory deficit per se.

Word Fluency

Successful performance on word fluency tests depends on the subject's ability to develop a strategy that facilitates the output of groups of meaningfully related words that allows keeping track of the words already spoken. Verbal fluency deficits have been shown to be sensitive to left frontal lobe lesions and more specifically the inferior frontal gyrus (Amunts, Weiss, Mohlberg, Pieperhoff, et al., 2004; Benton, 1968; Perret, 1974). The FAS Test asks the subject to provide as many words as possible in 1 minute beginning with the letter F (followed by A, followed by S). The category fluency test asks subjects to provide as many words as possible in 1 minute that belong to the category "animals" (then "food or drink"; Appendix K). Research associated with word generation found that patients with left-hemisphere lesions perform poorer than those with right focal lesions (Tucha, Smely, & Lange, 1999). Other reports have found verbal fluency tasks to be sensitive to frontal lobe damage irrespective of the side of the lesion

(Bruyer & Tuyumbu, 1980; Miceli, Caltagirone, Gainotti, Masullo, et al., 1981). Varley (1995) reported that category fluency was impaired in patients with right-hemisphere lesions only when generalized cognitive deficits were also present.

Stroop Test

The Stroop Color and Word Test is based on the observation that individuals can read words much faster than they can identify and name colors and it presents a measure of cognitive flexibility and resistance to interference from outside stimuli (Stroop, 1935). Performance on the Stroop test has been associated with activation of the anterior cingulate gyrus (Pardo et al., 1990). The test consists of a Word Page with rows of words printed in black and white (e.g., red, green, blue), a Colour Page with rectangles printed in red, green, or blue colour, and a Colour-Word Page with words printed in colour (e.g., word "red" printed in colour "blue," word "blue" printed in colour "red," etc.). The subject is asked to read words (Word Page) or name the colour of the ink (Colour Page) as quickly as possible within a 45 seconds time limit. On the Colour-Word Page, the subject is asked to complete an incongruous task by naming the colour in which words are written rather than read the words themselves (i.e., if the word green is displayed in colour blue, the correct response is "Blue"). The test yields three scores based on the number of items completed on each of the three stimulus sheets (Appendix L). Brown, Kindermann, Siegle, Granholm, et al. (1999) used blood oxygen level dependent (BOLD) functional magnetic resonance imaging (fMRI) to study the patterns of brain activation associated with performance on the Stroop Color–Word task. They reported

larger BOLD signal responses during the incongruous Stroop condition than during baseline conditions in several brain regions including the left- and right anterior cingulate, the right precuneus, and the left pars opercularis. Other research, however, has implicated prefrontal cortex rather that the anterior cingulate in the selection of task-relevant information required to complete the incongruous Stroop condition (Banich, Milham, Atchley, Cohen, et al., 2000; Perret, 1974; Vendrell, Junque, Pujol, Jurado, et al., 1995). In a review of the Stroop literature, MacLeod (1991) found that most models of Stroop interference predict a greater disturbance in the left rather than the right hemisphere due to the preferential role played by the left hemisphere in language-related processes making it more susceptible to verbal distractions.

Cambridge Neuropsychological Test Automated Battery (CANTAB)

CANTAB represents a collection of automated computerized material, mostly non-verbal, visually presented using a touch screen (CENES, 1999; Appendix M). It was designed to assist in dissociating frontal from temporal lobe behavioural functions, and as such, it measures a variety of cognitive abilities, including learning, memory, attention, problem solving, as well as 'executive' function and vigilance. The following subtests have been included: (1) Spatial Span; (2) Spatial Working Memory; (3) Paired Associates Learning; (4) Rapid Visual Information; (5) Match to Sample Visual Search Processing; (6) Intradimensional/Extradimensional (ID/ED) Set-Shifting; and (7) Stockings of Cambridge.

The Spatial Span subtest is based on the Corsi block task (Milner, 1971), and provides a measure of memory for a figural sequence. It is believed to activate the right ventrolateral prefrontal cortex (Robbins et al., 1996). On each trial, the subject views an array of 10 white boxes displayed on the computer screen. At the start of the task, two boxes change color sequentially. After the completion of the sequence, a beep signals that the subject can reproduce the sequence. Correct responding increases the level of difficulty up to a maximum sequence length of nine. Three attempts at each difficulty level are permitted before the test terminates. Prior to the start of test trials, two practice trials are given to assure the understanding of the task.

The Spatial Working Memory subtest is a self-ordered searching task (Petrides & Milner, 1982) that measures working memory for spatial stimuli and requires the subject to use mnemonic information to work towards a goal. Results from positron emission tomography imaging show activation of both the dorsal and ventral prefrontal regions (Owen, Evans & Petrides, 1996). On each trial, a number of coloured squares are displayed on the screen. By touching the right box, a blue token appears. The subject's task is to move the blue token to the empty black box displayed at the right of the screen. Each coloured square will contain only one token at some point in the course of a trial. A trial ends when all tokens are found. The subject ultimately completes four trials each with 2-items, 3-items, 4-items, 6-items, and 8-items. The colors and positions of the coloured squares change from trial-to-trial to discourage the use of stereotyped search strategies. In order to perform the task most efficiently without searching repeatedly in previously targeted locations, the subject must remember all the locations where a token

was found during each trial. The order in which the subject searches the coloured squares is self-determined. Returning to an 'empty' box already targeted on a particular search constitutes a 'forgetting' error. One strategy that has been defined as an effective one (Fray, Robbins & Sahakian, 1996; Owen, Downes, Sahakian, Polkey, & Robbins, 1990) is to follow a predetermined search sequence, beginning with a particular square and then, once a token is found, returning to that same starting point when initiating the next search. The extent to which this repetitive search strategy is used is estimated from the number of searches that start with the same location, within each of the 6-item and 8-item searches. A high score (many searches starting with different locations) indicates low use of this strategy while a low score (many searches starting with the same location) indicates more consistent use of this strategy.

The Visual Paired Associates Learning subtest examines the ability to form visuo-spatial associations. The number of correctly placed patterns for the first presentation of a trial provides an index of 'list memory' and the number of repeat trials needed to learn all the associations provide a measure of 'list learning.' The subject is required to remember patterns associated with different locations on the screen. During the test phase, the subject has to press the appropriate location upon the presentation of an item. Two trials of sets of one, two, three, six, and eight patterns are presented. The subject is allowed up to ten repeat presentations of a given set, before the task is terminated.

The Rapid Visual Information Processing subtest is a test of sustained attention with a small working memory component. A white box is presented on the computer

screen. Inside the box, digits from two to nine are presented sequentially in pseudo-random order at a rate of 100 digits per minute. The test lasts four minutes and includes a one-minute practice trial. Subjects are requested to detect and respond to consecutive even or odd sequences of digits (e.g., 2-4-6, 3-5-7, 4-6-8, and 5-7-9). The responses that occur within 1.8 seconds of the final presentation of the last digit of a target sequence are recorded. False alarms are also recorded and are defined as the instances when a subject incorrectly identifies a target sequence. The mean hit response latency is reported.

The Match to Sample Visual Search subtest tests the subject's ability to match visual samples by recording reaction and movement times. An abstract sample pattern is displayed in a red square, in the middle of the screen. After a brief delay, a varying number of similar patterns (i.e., 1, 2, 4, or 8) are shown in a circle around the edge of the screen. Only one of the patterns is a perfect match to the sample pattern, and the subject has to select matching pattern by releasing a press-pad and touching it on the screen. Reaction time is measured based on the release of the press-pad. Movement time is measured from the time when the press-pad was released and the first touch of the monitor screen.

The Intradimensional/Extradimensional (ID/ED) Set-Shifting subtest measures discrimination and reversal learning when the subject is required to shift attention to changing patterns of visual stimuli. The dorsolateral prefrontal cortex was found to be implicated in between-category set shifting while the orbitofrontal cortex was found to be associated with within-category reversal shifts in a lesion study in marmosets (Dias,

Robbins, & Roberts., 1996). The ID/ED task progresses along a series of stages of increasing difficulty. At the "simple discrimination" stage, the subject is presented with two lined patterns and is required to learn a two-alternative forced-choice discrimination using immediate feedback provided by the computer. The correct pattern is found by touching one pattern or the other. If correct, the computer will flash green; if incorrect, the computer will flash red. The next stage is introduced after six consecutive correct responses on the previous criterion. At the Simple Reversal stage, the feedback provided to each stimulus is reversed. At the third and forth stages, a shape element is added to the lined drawings. Two Compound Discrimination (CD) conditions are administered and the subject must continue to respond to the previously relevant lined drawing while ignoring the presence of the new irrelevant dimension. The fifth stage is a CD Reversal condition. The final condition is termed the intradimensional (ID) shift stage and it involves the first demand for an attentional shift. New examples of each of the two dimensions (line and shape) are introduced, and the subject must continue to respond to the previously relevant dimension (lined drawing). Success on this stage requires that the subject generalize previous learning to new stimuli. After a feedback reversal shift, the second demand for an attentional shift is introduced. This stage is termed the extradimensional shift and the subject must shift response set from the previously relevant dimension (lined drawing) to the previously irrelevant dimension (purple shape). Thus, the extradimensional shift requires the subject learn and respond to a new rule. Variables coded for each subject include the stage reached, the trials to criterion, and the number of error scores for each completed stage. A subject fails to reach criterion at a

particular stage after 50 trials during which no six consecutive correct responses were given.

The Stockings of Cambridge subtest is similar to Tower of London test (Shallice, 1982). The subject is presented with two displays that contain three coloured balls. The displays are presented in a way such that they may be perceived as stacks of coloured balls held on socks suspended from a beam. This particular presentation makes the 3-D concept of the task apparent to the subject and facilitates the verbal instructions. The subject is asked to use the balls in the lower display to reproduce the pattern shown in the upper display. The balls can be moved one at a time by first touching the required ball followed by the position where the ball should be moved. Two blocks of problems are presented. In the first block, the number of moves needed to complete a problem increases from one to four, while in the second block, the number of required moves increases from two to five moves. Immediately following each block of problems, a procedure designed to control for motor performance is inserted. The upper display moves one ball at a time, repeating the moves made by the subject in the corresponding problem solving phase. The subject is required to follow the upper display by moving the balls in the lower display. A problem is terminated if the subject makes more than double the number of moves required to complete the problem, and the subtest is terminated if the subject fails to solve three problems in a row. In the problem-solving phase, the time taken to complete a pattern and the number of moved made, are taken as indicators of the subject's planning ability. In the copying phase, the difference in time taken to complete and initiate each problem is taken as an index of additional time taken

to plan the solution of the copying. Research applying the task found bilateral activation of the parietal cortex in the excess number of moves needed to complete a problem, activation of the left caudate nucleus for the two-move problems, and activation of the dorsolateral prefrontal cortex, when completing three-move problems (Luciana & Nelson, 1998). Thinking latencies were proven useful in differentiating between patients with frontal lobe lesions and those with basal ganglia disorders (Owen, James, Leigh, Summers, Marsden, Quinn, Lange, & Robbins, 1992).

Tapping Test

The Tapping Test requires visuo-motor coordination (Thurstone, 1944). The test requires the subject to complete a sequential tapping sequence with each hand, as well as with both hands simultaneously. Each of these sequences is administered twice for 30 seconds. A one trial single tapping sequence with each hand is also included. Each single tapping trial lasts 15 seconds (Appendix N). Leonard, Milner, & Jones (1988) reported superior results on simple and sequential tapping using the right hand irrespective of the presence of lesion hemispheric location. Female patients with either left (LF) or right frontal (RF) lobe lesions were found to perform slower than the normal control subjects on simple tapping, and both male and female patients with LF and RF lesions were impaired on both hands relative to the normal control subjects on sequential tapping.

Grooved Pegboard Test

The Grooved Pegboard is a manipulative dexterity test consisting of a 5x5 matrix of keyhole shaped holes in various orientations (Lafayette Instrument Company; Trites, 1995). Pegs with a key along one side must be rotated to match the hole before they can be inserted. The score for the Grooved Pegboard was the amount of time required to complete the task, including the additional time in the event the subject dropped a peg or more. This test is used to evaluate lateralized brain damage and requires complex visual-motor coordination (Appendix O). Investigation of manual motor asymmetries using the Grooved pegboard test in patients with unilateral left- or right hemisphere lesions revealed contralateral motor deficits for both groups of patients as well as ipsilateral deficits for the patients with left hemisphere lesions (Hanna-Pladdy, Mendoza, Apostolos, & Heilman, 2002).

Pinch Strength Test

The Pinch Dynamometer test provides a measure of finger strength (Kellor, Frost, Silberberg, Iversen, & Cummings, 1971). Subjects are instructed to pinch as hard as possible the pinch dynamometer between the index finger and the thumb. Three trials with each hand are administered and the final score for each hand is the mean of the three trials (Appendix P). Data from individuals with unilateral cerebrovascular accident provides evidence for diminished strength both contralateral and ipsilateral to the hemisphere of lesion (Robinson, Fitts, & Kraft, 1990).

Data Statistical Analyses

The emotional state, personality, and neuropsychological data were evaluated using various statistical analyses. The results were evaluated using the Statistical Package for the Social Sciences (SPSS/PC; Nie, Hadlai, Jenkins, Steinbrenner, & Bent, 1970). Means and standard deviations for the groups were calculated for the demographic, neuropsychological, and self-report variables. Group differences for the entire testing battery were investigated using univariate ANOVAs to determine the specific tests on which the groups differed. The level of significance was set at $p \leq .05$, and post hoc contrasts were applied to evaluate the data set.

Sample Size, Type I Error, Type II Error, and Power

The interpretation of results for neuropsychological studies that investigate differences between normal control subjects and clinical populations (including migraine patients) is difficult because of the inclusion of small sample sizes, the large number of dependent variables, and the use of multiple univariate statistical analyses that rely upon multiple t-tests. These latter factors contribute to an increased probability of committing a Type I error or the false rejection of the null hypothesis or the hypothesis, which states that the groups do not differ significantly. Traditionally, alpha corrections such as the Bonferroni correction have been used to reduce the probability of Type I error, however such procedures have the consequence of limiting the statistical power and increasing the Type II error, which influences the ability to detect differences "true" between the groups (Cohen, 1992).

In the present study, the identification of differences between the neuropsychological profiles of migraine patients and healthy control subjects is unfortunately reliant upon the use of an extensive battery of tests that correlate with many functional domains. The sample size required to achieve an adequate level of statistical power in such research would need to be very high and consequently, difficult to attain because this population is often diagnosed with comorbid psychiatric conditions such as anxiety and depression.

The use of planned comparisons is a useful method for reducing the Type I error because it limits the number of required statistical analyses, however, such an approach, is not ideal when the scope of the study includes the evaluation of differential group deficits. Another possibility is to group tests into functional domains and to conduct separate analyses for each domain, which results in fewer univariate statistical tests and consequently reduces the level Type I error (Miller & Rohling, 2001).

Composite Neuropsychological Indices

In addition, tests were grouped according to specific cognitive functioning domains. The nine groupings relied on previously published data (Larrabee, Kane, & Schuck 1983; Leonberger, Nicks, Larrabee, & Goldfader, 1992; Lezak, 1995; Nicks, Leonberger, Munz, & Goldfader, 1992; Robertson, Ward, Ridgeway, & Nimmo-Smith, 1996; Shute & Huertas, 1990; Spreen & Strauss, 1998). ANOVAs were performed to

determine whether the subject groups differed in their performance on any of the cognitive composite domains.

Attention & Concentration Composite Index: WMS-III Digit Span Forward subtest; CANTAB Spatial Span; CANTAB Rapid Visual Processing; Stroop test Colour subtest; Stroop test Word subtest.

Verbal Memory Composite Index: WMS-R Logical Memory subtest mean number of items recalled on each of the two prose passages immediately after their presentation and following a time delay; CVLT-II free and cued recall items immediately after their presentation and following a time delay.

Visuo-Spatial Memory Composite Index: Rey-Osterreith Complex Figure immediate and delayed recall scores and time taken to reproduce the design; WMS-III Faces subtest number of correctly identified unfamiliar faces immediately after presentation and following a time delay.

Working Memory Composite Index: Number of between-trial errors on the CANTAB Spatial Working Memory subtest; number of recall errors on the CANTAB Paired Associate Learning; WMS-III Letter Number Sequencing subtest score; span length for the WMS-III Digit Span Backward subtest.

Verbal Expression Composite Index: WASI Vocabulary T score; number of words produced on the semantic (Animal and Food & Drink words) and phonemic (Letter F; Letter S; and Letter A words) trials of the Word Fluency test.

Constructional Abilities Composite Index: WASI Block Design T score; Rey-Osterreith Complex Figure copy score and the time taken to complete the design.

Executive Functioning Composite Index: CANTAB Intra/Extra Dimensional subtest stages achieved and total number of set shifting errors; CANTAB Stockings of Cambridge subtest initial and subsequent thinking times and total problems solved with a minimum number of moves; CANTAB Spatial Working Memory strategy score; Stroop test Colour-Word subtest score.

General Cognitive Index: FSIQ; VIQ; PIQ; Attention & Concentration, Verbal Fluency, Constructional Abilities, Executive Functioning, Verbal, Visuo-Spatial, and Working Memory composite scores.

Motor Functioning Composite Indices: Separate indices were derived for each hand. Mean performance on the Tapping test: right and left hand scores for sequential and single tapping; Grooved Pegboard test: right and left hand mean results, and Pinch Test: right and left hand mean results.

RESULTS

The normal control subjects were matched to the migraine patients with (MA) and without aura (MO) for age, hand preference, and years of education. Although all the groups were matched for hand preference, given the important role played by handedness on the hemispheric lateralization of language, data from left-handed and ambidextrous individuals (n = 8) were not included in statistical analyses. Table 4 presents means and standard deviations for right-handed normal control subjects (n = 10) and migraine patients with (n = 12) and without (n = 17) aura for age, hand preference, and years of education. The migraine patient groups were divided according to the presence or absence of aura symptoms, and the hemispheric localization of the migraine pain. Group differences were evaluated using one-way ANOVA and results were considered significant at $p < .05$. The 'Observed Power' column included in the ANOVA tables provides an indication of the ability of the statistical method employed to detect group differences. This value is computed by the SPSS statistical package using the number of subjects in the groups, the observed mean difference between groups and the standard deviations of the groups. Thomas and Krebs (1997) argued that if the value of the observed power is low, this provides insufficient evidence in favor of the null hypothesis (i.e., no group differences).

No significant group differences were noted, confirming that the groups were well matched on these characteristics (Table 5). The group of normal control subjects included four males while the migraine patient groups included three. To ensure that

gender did not influence performance in this study, preliminary analyses were carried out separately for groups with and without the male subjects. No significant differences in performance on several measures of interest including overall level of cognitive abilities, memory abilities, and attention and concentration were revealed and therefore all analyses were collapsed across gender. Although for the motor tests, results were not statistically different when both genders were included, final analyses present data only from female subjects.

Table 4

Means and standard deviations for demographic characteristics of right-handed subjects

Characteristic	N	Mean	SD
Age			
NC[1]	10	37.10	12.79
MO_{Right}	10	46.80	10.18
MO_{Left}	7	41.71	10.78
MA_{Right}	7	40.14	11.87
MA_{Left}	5	39.20	11.21
Handedness Score			
NC	10	19.80	2.04
MO_{Right}	10	21.00	3.71
MO_{Left}	7	19.00	1.29
MA_{Right}	7	19.71	2.98
MA_{Left}	5	20.20	3.49
Years of Education			
NC	10	15.10	2.81
MO_{Right}	10	15.40	2.01
MO_{Left}	7	14.57	3.21
MA_{Right}	7	13.43	2.44
MA_{Left}	5	15.00	2.65

Note. [1]NC = Normal control subjects; MO_{Right} = migraine patients without aura with right-sided headaches; MO_{Left} = migraine patients without aura with left-sided headaches; MA_{Right} = migraine patients with aura with right-sided headaches; MA_{Left} = migraine patients with aura with left-sided headaches.

Table 5

One-way ANOVA for equality of means on demographic characteristics of right-handed subjects

Variable	df	SS	MS	F	p	Power
Age						
Group[1]	4	511.34	127.83	0.98	0.433	0.28
Hemisphere[2]	2	255.58	127.79	0.98	0.387	0.21
Type[3]	2	347.41	173.70	1.33	0.279	0.27
Handedness Score						
Group	4	18.17	4.54	0.56	0.690	0.17
Hemisphere	2	4.35	2.18	0.27	0.765	0.09
Type	2	0.26	0.13	0.02	0.984	0.05
Years of Education						
Group	4	18.19	4.55	0.66	0.621	0.19
Hemisphere	2	3.03	1.51	0.22	0.803	0.08
Type	2	5.45	2.73	0.40	0.674	0.11

Note. [1]'Group' Classification: Normal control subjects; migraine patients without aura with right-sided headaches; migraine patients without aura with left-sided headaches; migraine patients with aura with right-sided headaches; migraine patients with aura with left-sided headaches.

[2]'Hemisphere' Classification: Normal control subjects; migraine patients with right-sided headaches; migraine patients with left-sided headaches.

[3]'Type' Classification: Normal control subjects; migraine patients without aura; migraine patients with aura.

Emotional Status and Personality Traits

The Beck Depression and the State Trait Anxiety inventories were completed by the migraine patients and the normal control subjects to ensure that they neither were depressed nor had significantly raised anxiety. Statistical analyses confirmed that no significant differences were present on these scales and the means and standard deviations are presented in Appendix Q (Table Q-1 and Table Q-2).

Personality Characteristics

Group differences were present on two NEO-PI subscales, Neuroticism and Openness to Experience suggesting that migraine diagnosis increases the likelihood of reacting strongly to distressing circumstances and diminishes an individual's ability to handle emotions adequately (Table 6).

Table 6

Personality Characteristics: ANOVA Results

Variable	df	SS	MS	F	p	Power
NEOPI-N						
Group	4	5990.85	1497.71	2.67	0.049*	0.68
Hemisphere	2	3447.16	1723.58	3.07	0.059	0.56
Type	2	5709.62	2854.81	5.09	0.012*	0.79
NEOPI-O						
Group	4	4276.75	1069.19	4.56	0.005**	0.91
Hemisphere	2	4138.86	2069.43	8.83	0.001***	0.96
Type	2	2516.26	1258.13	5.37	0.009**	0.81

Note. *p< .05; **p< .01; ***p< .001.

Post-hoc contrasts for the NEO-PI Neuroticism and Openness to Experience subscales are presented in Table 7. MA and M_{Left} were associated with a higher propensity toward strong emotional reactivity than NC and MO. On the Neuroticism scale, low scores are associated with calm and confident personalities and high scores correlate with increased levels of self-consciousness, impulsiveness, and vulnerability. The normal control subjects ($\underline{M}$ = 73.30, $\underline{SD}$ = 29.74) obtained significantly lower scores than the MA ($\underline{M}$ = 103.75, $\underline{SD}$ = 22.85) and M_{Left} ($\underline{M}$ = 96.26, $\underline{SD}$ = 21.65) patients. The MO patients ($\underline{M}$ = 83.03, $\underline{SD}$ = 19.1) obtained significantly lower scores than the MA patients. The mean scores in Figure 1 depict the association between migraine with aura, hemispheric lateralization of migraine and personality characteristics on the Neuroticism subscale.

On the Openness to Experience subscale, the normal control subjects (M = 128.00, SD = 11.53) scored significantly higher than the MO (M = 109.13, SD = 17.89), MA (M = 107.44, SD = 16.67), and M_{Right} (M = 102.64, SD = 15.71) patients. High scores are associated with imaginative personalities and low scores correlate with conventional, conservative response styles. The M_{Left} patients (M = 116.64, SD =16.16) obtained significantly higher scores on the Openness to Experience scale than the M_{Right} patients. The mean scores in Figure 2 depict the association between migraine with aura, hemispheric lateralization of migraine and personality characteristics on the Openness to Experience subscale. In general, patients with migraine reported elevated emotional reactions to stressful events and relatively more conservative response styles than those of healthy control subjects.

Table 7

Personality Characteristics: Post-hoc Contrast Tests

Variable[1]	Contrast	Contrast Value[2]	Std. Error	t	p
NEO-PI N					
	NC vs. MO	-20.47	18.98	-1.08	0.289
	NC vs. MA	-62.72	20.41	-3.07	0.004**
	NC vs. M_{Right}	-33.30	18.98	-1.75	0.088
	NC vs. M_{Left}	-49.89	20.41	-2.44	0.020*
	M_{Right} vs. M_{Left}	-16.59	18.12	-0.92	0.366
	MO vs. MA	-42.25	18.12	-2.33	0.026*
NEO-PI O					
	NC vs. MO	34.96	12.27	2.85	0.007**
	NC vs. MA	39.18	13.19	2.97	0.005**
	NC vs. M_{Right}	50.74	12.27	4.13	0.000***
	NC vs. M_{Left}	23.41	13.19	1.77	0.085
	M_{Right} vs. M_{Left}	-27.33	11.71	-2.33	0.026*
	MO vs. MA	4.22	11.71	0.36	0.721

Note. [1]NEO-PI N = Neuroticism subscale of the NEO-PI; NEO-PI O = Openness to experience subscale of the NEO-PI.

[2]df= 4, 34.

*p< .05; **p< .01; ***p< .001.

Figure 1. Group Means for the NEO-PI Neuroticism Subscale

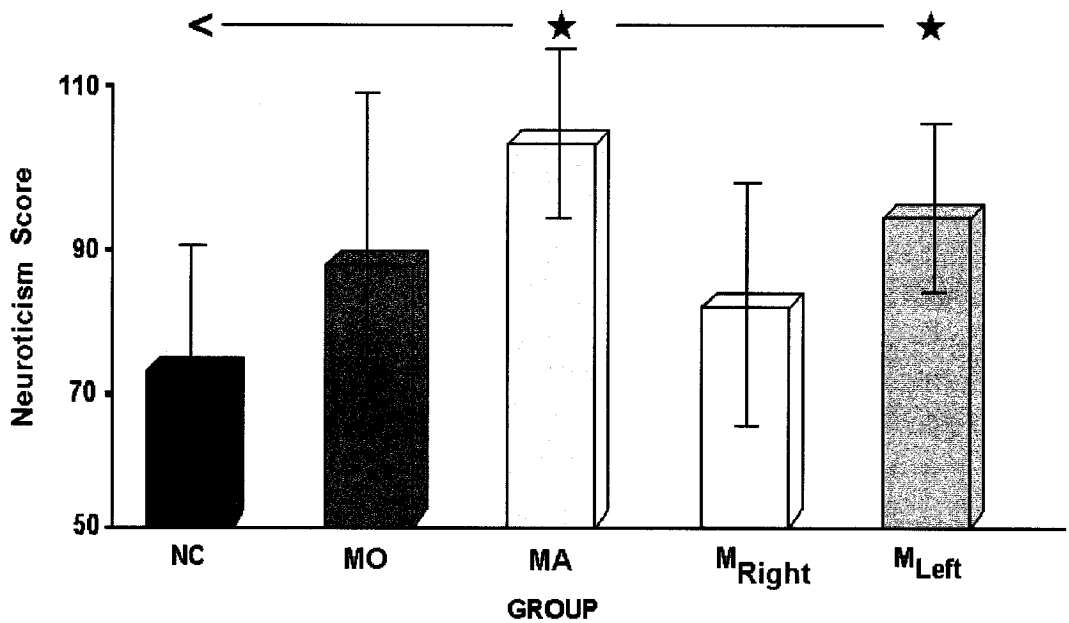
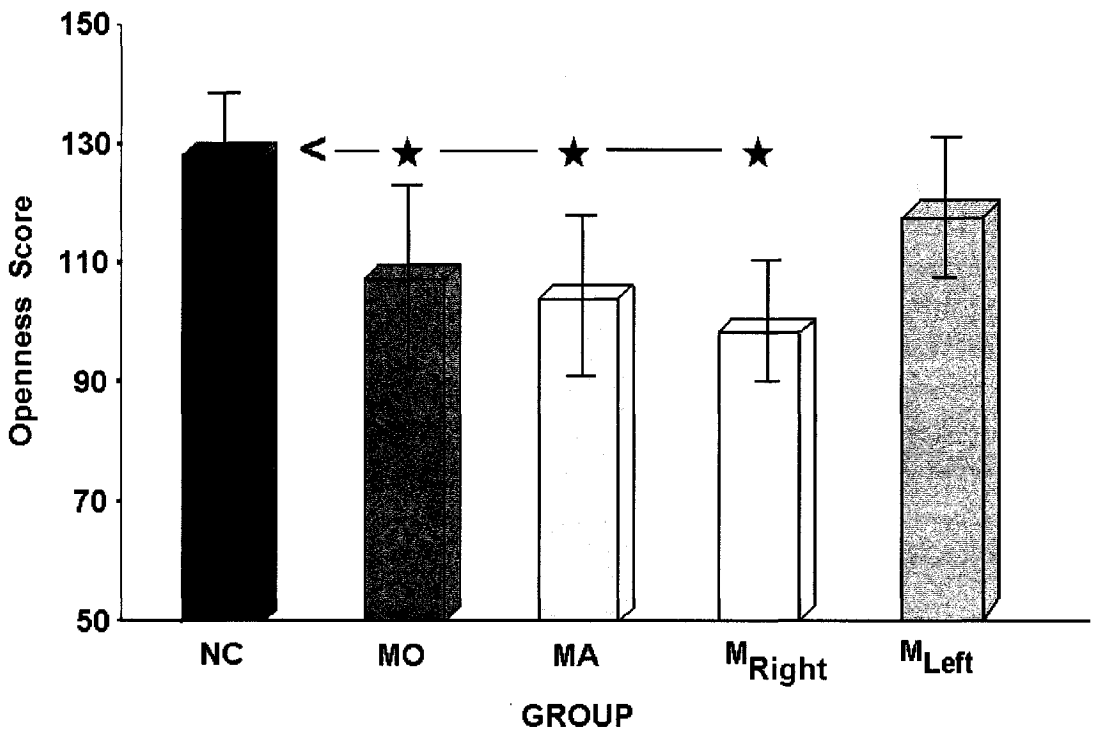

Neuroticism Score
110
90
70
50
NC
MO
MA
M Right
M Left
GROUP

Figure 2. Group Means for the NEO-PI Openness to Experience Subscale


150
130
110
90
70
50
Openness Score
NC
MO
MA
M Right
M Left
GROUP

Statistical Analyses of Individual Neuropsychological Measures

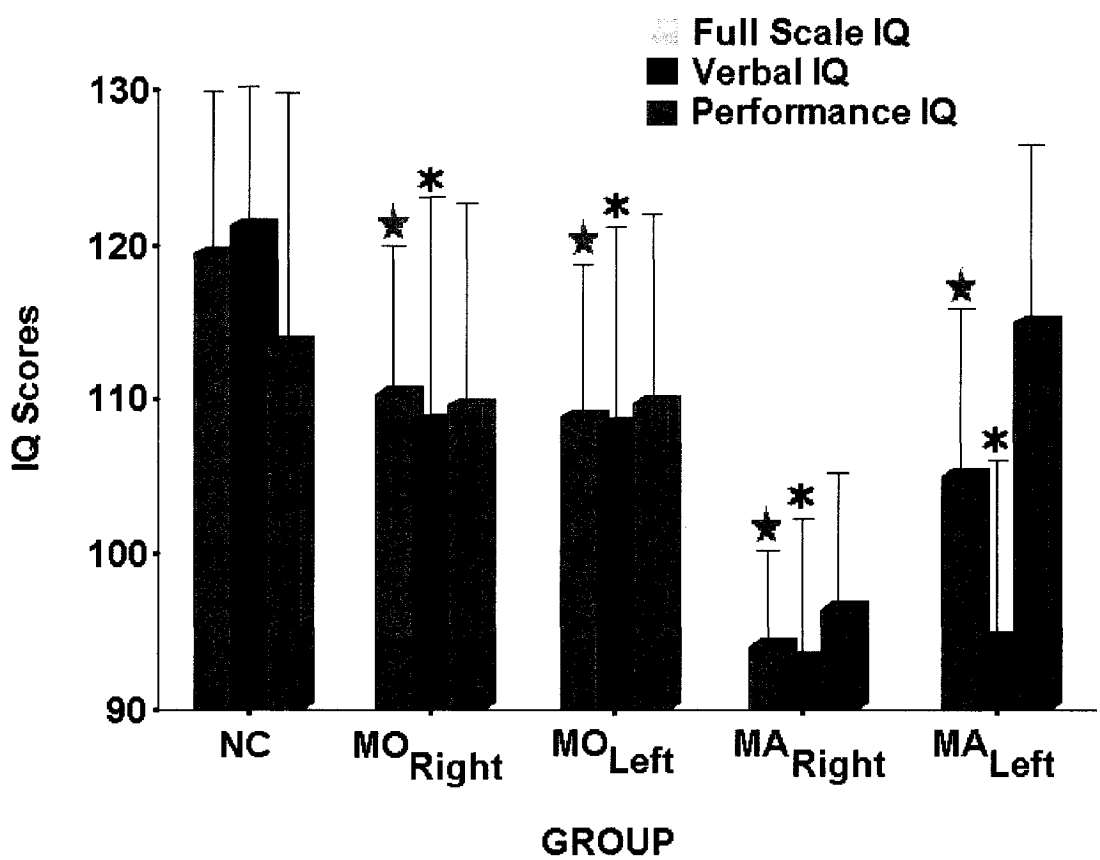
Neuropsychological data were analyzed using several statistical approaches. The first procedure assessed group differences for individual neuropsychological measures using univariate ANOVAs while a second method relied on grouping of neuropsychological variables into cognitive domains. In order to determine which specific groups differed, significant ANOVAs were followed by planned post-hoc contrasts between normal control subjects, migraine with and without aura, and migraine lateralized over the left- and right cerebral hemisphere.

Means and standard deviations for individual psychological measures for the normal control subjects and patients diagnosed with migraine with- and without aura, sub-grouped by migraine cerebral hemisphere localization are found in Appendix R (Tables R-1 through R-9). Statistical analyses were performed for overall cognitive abilities including Full Scale, Verbal, and Performance IQ estimates; attention and concentration; memory; executive function; and motor abilities.

Overall Cognitive Abilities

The Wechsler Abbreviated Scale of Intelligence (WASI) was used to provide a baseline of overall verbal and visual-spatial abilities. Means for the Full Scale IQ, Verbal IQ, and Performance IQ ratings, for all the groups are shown in Figure 3.

Figure 3. Full Scale IQ, Verbal IQ, and Performance IQ Ratings: Group Means


Full Scale IQ
Verbal IQ
Performance IQ
130
120
110
100
90
IQ Scores
NC
MO Right
MO Left
MA Right
MA Left
GROUP

The analysis of variance (ANOVA) results for measures of intellectual function yielded group differences for the Full Scale (FSIQ) and Verbal IQ (VIQ) scores (Table 8). Post-hoc contrasts for FSIQ and VIQ scores revealed no effect of the hemispheric localization of migraine but a superior performance of the normal control subjects as compared to MO and MA patients (Table 9). Migraine aura was associated with significantly poorer performance than MO. For FSIQ the normal control subjects (M = 119.4, SD = 12.47) obtained significantly higher scores than the MO patients (M = 109.71, SD = 9.94) who obtained significantly higher results than the MA patients (M = 98.67, SD = 10.32) whether the headache pain was localized over the right- (M = 103.65, SD = 12.12) or the left (M = 107.25, SD = 10.30) cerebral hemisphere.

Similarly, for VIQ the normal control subjects (M = 121.2, SD = 11.04) obtained significantly higher scores than the MO (M = 108.41, SD = 15.11) and MA patients (M = 93.83, SD = 12.32) irrespective of whether the headache pain was localized over the right (M = 102.24, SD = 15.96), or left (M = 102.58, SD = 15.79) hemisphere. Interestingly, statistical analyses for the Performance IQ ratings did not reveal any significant differences in performance between migraine and healthy control subjects, raising the possibility that the significant differences seen on the Full Scale IQ ratings were primarily driven by verbal rather than visuospatial abilities.

Examination of the mean IQ ratings presented in Figure 3, leads us to speculate that a diagnosis of MA_{Right} could ultimately be associated with diminished verbal and visuospatial abilities while MA_{Left} presents lower verbal but intact visuo-spatial abilities.

The investigation of the Verbal IQ versus Performance IQ difference was carried out using independent-sample t-tests for the (1) normal control subjects versus MO_{Right} and MO_{Left}; (2) normal control subjects versus MA_{Right} and MA_{Left}; (3) MO_{Right} versus MO_{Left}; and (4) MA_{Right} versus MA_{Left}. The difference between the Verbal and Performance IQ ratings for the normal control subjects ($\underline{M}$ = 7.60; $\underline{SD}$ = 16.27) versus the MA_{Left} patients ($\underline{M}$ = -20.40; $\underline{SD}$ = 18.93) was significant ($t = 2.98$, $p < 0.05$). The normal control subjects obtained an average of 8 points higher Verbal than Performance IQ ratings while the MA_{Left} patients showed a reversed pattern with an average of over 20 points lower Verbal than Performance IQ ratings.

Table 8

General Intellectual Abilities: ANOVA Results

Variable	df	SS	MS	F	p	Power
FSIQ						
Group	4	2722.14	680.54	6.10	0.001***	0.97
Hemisphere	2	1861.93	930.96	8.34	0.001***	0.95
Type	2	2123.93	1061.96	9.51	0.001***	0.97
VIQ						
Group	4	4134.20	1033.55	5.48	0.002**	0.96
Hemisphere	2	2976.61	1488.31	7.89	0.002**	0.94
Type	2	4033.22	2016.61	10.69	0.000***	0.98
Vocabulary						
Group	4	1774.54	443.64	3.58	0.015*	0.82
Hemisphere	2	1318.96	659.48	5.32	0.010**	0.80
Type	2	1731.42	865.71	6.98	0.003**	0.90
Similarities						
Group	4	1389.81	347.45	5.32	0.002**	0.95
Hemisphere	2	847.86	423.93	6.49	0.004**	0.88
Type	2	1340.02	670.01	10.25	0.000***	0.98
PIQ						
Group	4	1505.03	376.26	2.23	0.087	0.59
Hemisphere	2	928.49	464.24	2.75	0.078	0.51
Type	2	335.70	167.85	0.99	0.381	0.21
Block Design						
Group	4	513.13	128.28	1.41	0.252	0.39
Hemisphere	2	365.06	182.53	2.00	0.150	0.38
Type	2	236.69	118.34	1.30	0.286	0.26
Matrix Reasoning						
Group	4	626.80	156.70	2.25	0.085	0.59
Hemisphere	2	284.02	142.01	2.04	0.146	0.39
Type	2	69.33	34.66	0.50	0.613	0.12

Note. *p< .05; *p< .01; ***p< .001.

Table 9

FSIQ and VIQ: Post-hoc Contrast Tests

Variable	Contrast[1]	Contrast Value[2]	Std. Error	t	p
FSIQ					
	NC vs. MO	19.64	8.47	2.32	0.027*
	NC vs. MA	39.66	9.11	4.35	0.000***
	NC vs. M_{Right}	34.36	8.47	4.06	0.000***
	NC vs. M_{Left}	24.94	9.11	2.74	0.010**
	M_{Right} vs. M_{Left}	-9.41	8.09	-1.16	0.252
	MO vs. MA	20.01	8.09	2.47	0.018*
VIQ					
	NC vs. MO	25.61	11.01	2.33	0.026*
	NC vs. MA	54.51	11.84	4.60	0.000***
	NC vs. M_{Right}	40.61	11.01	3.69	0.001***
	NC vs. M_{Left}	39.51	11.84	3.34	0.002**
	M_{Right} vs. M_{Left}	-1.10	10.51	-0.10	0.917
	MO vs. MA	28.90	10.51	2.75	0.010**

Note. [1]NC = Normal control subjects; MO = migraine patients without aura; MA = migraine patients with aura; M_{Right} = patients with right-sided migraine; M_{Left} = patients with left-sided migraine.

[2]df= 4, 34.

*p< .05; *p< .01; ***p< .001.

Attention & Concentration

The tests selected for this investigation have been found to correlate with attentional processes associated with the functioning of both cerebral hemispheres: WMS-III Digit Span – forward (actual span forward), CANTAB Block Span - forward, CANTAB Rapid Visual Information Processing, and Stroop Test Number of Colours and Number of Words named (Hale et al., 2002; MacLeod, 1991; Robbins et al., 1996). Table 10 presents significant ANOVA results while non-significant findings are found in Appendix S (Table S-1). Post-hoc contrasts for Digit and Spatial Span forward (Table 11) revealed significantly longer digit span for the normal control subjects ($\underline{M}$ = 7.30, $\underline{SD}$ = 0.95) than the MO ($\underline{M}$ = 6.24, $\underline{SD}$ = 0.75) and M_{Right} patients ($\underline{M}$ = 6.29, $\underline{SD}$ = 0.69). For Spatial Span forward MA patients ($\underline{M}$ = 6.85, $\underline{SD}$ = 1.40) had significantly longer span than either the normal control subjects ($\underline{M}$ = 6.14, $\underline{SD}$ = 1.37) or the MO patients ($\underline{M}$ = 6.21, $\underline{SD}$ = 0.64). This advantage for simple attention demonstrated by the migraine with aura group may suggest a baseline state of heightened awareness of immediate surroundings that could facilitate the processing of simple stimuli and is consistent with a brain hyperexcitability hypothesis (Conlon & Humphreys, 2000; Wray et al., 1995).

Table 10

Attention & Concentration Processes: ANOVA Results

Variable	df	SS	MS	F	p	Power
Digit Span Forward						
Group	4	8.75	2.19	2.81	0.041*	0.70
Hemisphere	2	6.40	3.20	4.10	0.025*	0.69
Type	2	7.24	3.62	4.65	0.016*	0.75
Spatial Span Forward						
Group	4	12.52	3.13	2.95	0.034*	0.73
Hemisphere	2	4.94	2.47	2.33	0.113	0.44
Type	2	8.87	4.43	4.19	0.024*	0.70

Note. *$p < .05$.

Table 11

Attention & Concentration Processes: Post-hoc Contrast Tests

Variable[1]	Contrast	Contrast Value[2]	Std. Error	t	p
DgSpF					
	NC vs. MO	2.16	0.71	3.05	0.004**
	NC vs. MA	1.31	0.76	1.73	0.093
	NC vs. M_{Right}	2.01	0.71	2.85	0.007**
	NC vs. M_{Left}	1.46	0.76	1.92	0.064
	M_{Right} vs. M_{Left}	-0.56	0.68	-0.82	0.415
	MO vs. MA	-0.84	0.68	-1.25	0.221
SpSpF					
	NC vs. MO	0.11	0.83	0.14	0.892
	NC vs. MA	-2.02	0.89	-2.28	0.029*
	NC vs. M_{Right}	-0.22	0.83	-0.27	0.791
	NC vs. M_{Left}	-1.69	0.89	-1.90	0.066
	M_{Right} vs. M_{Left}	-1.47	0.79	-1.86	0.071
	MO vs. MA	-2.13	0.79	-2.71	0.011*

Note. [1]DgSpF = Digit Span Forward – Span Length; SpSpF = Spatial Span Forward – Span Length.

[2]$df = 4, 34$.

*$p < .05$; **$p < .01$.

Memory

The tests of verbal memory selected for this study included the CVLT-II and the WMS-III Stories. For visuo-spatial memory, we used the recall trials of the Rey-Osterreith Complex figure and the WMS-III Faces subtest. For the working memory, the WAIS-III Digit Span Backward (Span Length), WMS-III Letter-Number Sequencing subtest, CANTAB Spatial Working Memory and Visual Paired Associate Learning were employed. No significant differences were revealed for verbal and working memory measures (Appendix S, Tables S-2 through S-4), but the time taken to complete the immediate recall of the Rey Complex Figure as well as its delayed recall resulted in significant differences between the normal control subjects and migraine patients (Table 12). Post-hoc investigation of these differences revealed that the normal control subjects ($\underline{M}$ = 149.40, $\underline{SD}$ = 30.46) and the M_{Left} patients ($\underline{M}$ = 145.75, $\underline{SD}$ = 37.18) spent significantly longer time on the immediate recall of the Rey Figure than the M_{Right} patients ($\underline{M}$ = 120.59, $\underline{SD}$ = 32.00; Table 13). Figure 4 presents the mean results for the completion time on the immediate recall of the Rey Figure and the scores obtained on the delayed recall trial. Post-hoc comparisons for the delayed recall results of the Rey Figure showed that the normal control subjects ($\underline{M}$ = 15.80, $\underline{SD}$ = 5.00) obtained significantly higher scores than the M_{Right} patients ($\underline{M}$ = 10.53, $\underline{SD}$ = 4.33) who spent a significantly shorter time on the immediate recall trial of this figure.

Table 12

Visuo-Spatial Memory: ANOVA Results

Variable	df	SS	MS	F	p	Power
Rey Figure Immediate Recall Time (sec)						
Group	4	13899.27	3474.82	3.06	0.030*	0.75
Hemisphere	2	9031.44	4515.72	3.97	0.028*	0.67
Type	2	2598.14	1299.07	1.14	0.331	0.23
Rey Figure Delayed Recall						
Group	4	183.21	45.80	1.89	0.136	0.51
Hemisphere	2	177.05	88.53	3.65	0.037*	0.63
Type	2	112.56	56.28	2.32	0.114	0.44

Note. *$p < .05$.

Table 13

Visuo-Spatial Memory: Post-hoc Contrast Tests

Variable[1]	Contrast	Contrast Value	Std. Error	t	p
Rey IR (sec)					
	NC vs. MO	24.60[2]	27.03	0.91	0.369
	NC vs. MA	43.91	29.05	1.512	0.140
	NC vs. M_{Right}	64.31	27.03	2.38	0.023*
	NC vs. M_{Left}	4.20	29.05	0.14	0.886
	M_{Right} vs. M_{Left}	-60.11	25.80	-2.33	0.026*
	MO vs. MA	19.31	25.80	0.75	0.459
Rey DR					
	NC vs. M_{Right}	5.27[3]	1.91	2.758	0.009**
	NC vs. M_{Left}	2.47	2.05	1.201	0.238
	M_{Right} vs. M_{Left}	-2.80	1.81	-1.55	0.130

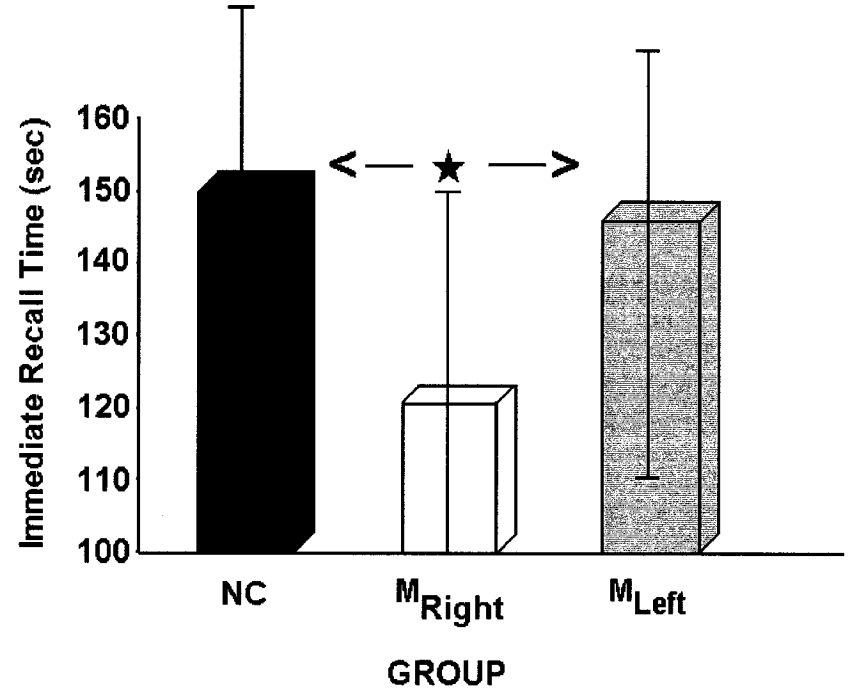
Note. [1]Rey IR (sec) = Time taken to complete the immediate recall trial of the Rey complex figure; Rey DR = Delayed recall trial of the Rey complex figure.

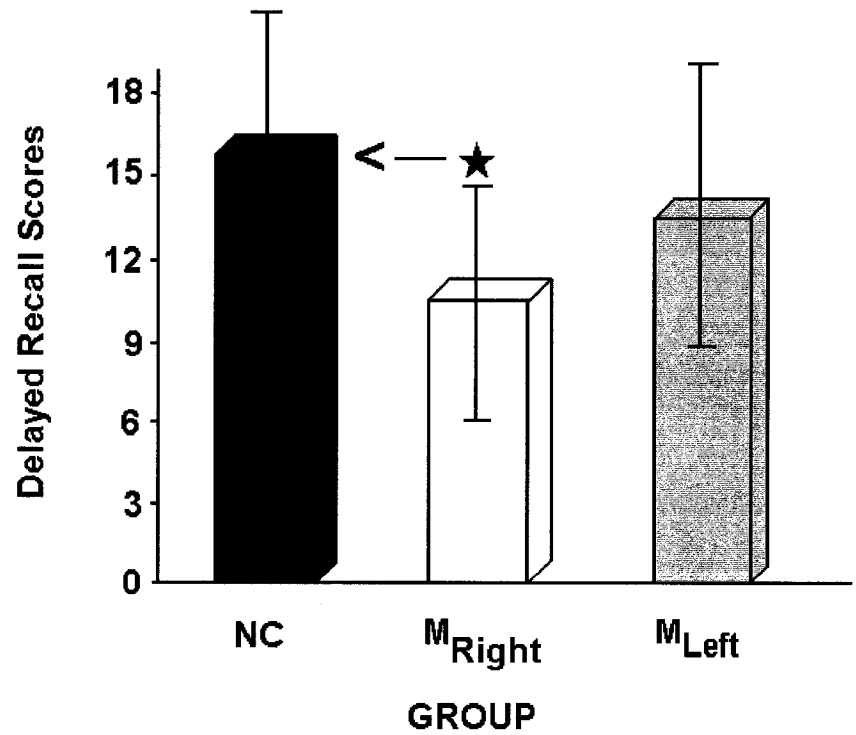
[2]df= 4, 34.

[3]df= 2, 36.

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

Figure 4. Group Performance on the Rey Complex Figure


Immediate Recall Time (sec)
160
150
140
130
120
110
100
NC
M Right
M Left
GROUP


Delayed Recall Scores
18
15
12
9
6
3
0
NC
M Right
M Left
GROUP

Executive Function

Tests associated with executive functioning selected for this study included the Stroop test and several subtests of the CANTAB: Spatial Working Memory Strategy, Intradimensional/Extradimensional (ID/ED) Set-Shifting, and Stockings of Cambridge (Table 14; Tables S-5 through S-7). Normal control subjects and migraine patients differed in their performance on the effective use of an optimal strategy for the completion of the spatial working memory subtest of CANTAB and for the time taken to complete the Tower of London subtest once the first move (thinking time) was initiated (Table 15). The optimal search strategy for the spatial working memory subtest relies on the repetition of an arbitrary search sequence until successful retrieval of all the searched items (CENES, 1999). The normal control subjects ($\underline{M}$ = 29.92, $\underline{SD}$ = 5.80) were significantly more likely to apply the optimal search strategy than MO ($\underline{M}$ = 33.28, $\underline{SD}$ = 3.63) or M_{Right} ($\underline{M}$ = 32.04, $\underline{SD}$ = 3.82) patients. The application of an optimal search strategy is typically associated with fewer errors and, as illustrated in Figure 5, despite the lack of significant statistical differences in the number of errors between groups, the normal control subjects averaged about 21 errors on this task whereas the MO and M_{Right} patients averaged 26 and 25 errors, respectively.

Post-hoc comparisons of the time taken to complete the Tower of London problems once the initial time associated with the first move was taken into account, revealed that the MA patients ($\underline{M}$ = 0.62, $\underline{SD}$ = 0.48) took significantly less time to complete problems than did the MO patients ($\underline{M}$ = 1.65, $\underline{SD}$ = 1.19). No significant

difference was present between the normal control subjects (M = 1.33, SD = 1.19) and the migraine patients for the completion time. It may be anticipated that such behaviour could lead to either improved performance as measured by the successful completion of problems with a minimum number of moves or conversely, it might lead to increased errors associated with insufficient allocation of resources for the on-line verification of the response correctness. These hypotheses, however, could not be verified by the data from this study, which failed to reveal any difference in the total number of problems solved with a minimum of moves between the MO and MA patients.

Table 14

Executive Function: ANOVA Results

Variable	df	SS	MS	F	p	Power
Spatial Working Memory – Strategy						
Group	4	190.86	47.71	2.90	0.036*	0.72
Hemisphere	2	76.38	38.19	2.32	0.114	0.44
Type	2	105.06	52.53	3.19	0.054	0.57
Tower of London – Subsequent Thinking Time (sec)						
Group	4	9.09	2.27	2.14	0.097	0.57
Hemisphere	2	1.77	0.88	0.83	0.444	0.18
Type	2	7.81	3.91	3.68	0.036*	0.64

Note. *p< .05.

Table 15

Executive Function: Post-hoc Contrast Tests

Variable[1]	Contrast	Contrast Value	Std. Error	t	p
SWM-Strategy					
	NC vs. MO	-7.73[2]	3.25	-2.38	0.023*
	NC vs. MA	-2.35	3.50	-0.67	0.505
	NC vs. M_{Right}	-6.89	3.25	-2.12	0.041*
	NC vs. M_{Left}	-3.19	3.50	-0.91	0.369
	M_{Right} vs. M_{Left}	3.71	3.10	1.19	0.241
	MO vs. MA	5.37	3.10	1.73	0.093
SOC STT (sec)					
	NC vs. MO	-0.32[3]	0.41	-0.78	0.438
	NC vs. MA	0.71	0.44	1.61	0.116
	MO vs. MA	1.03	0.39	2.66	0.012*

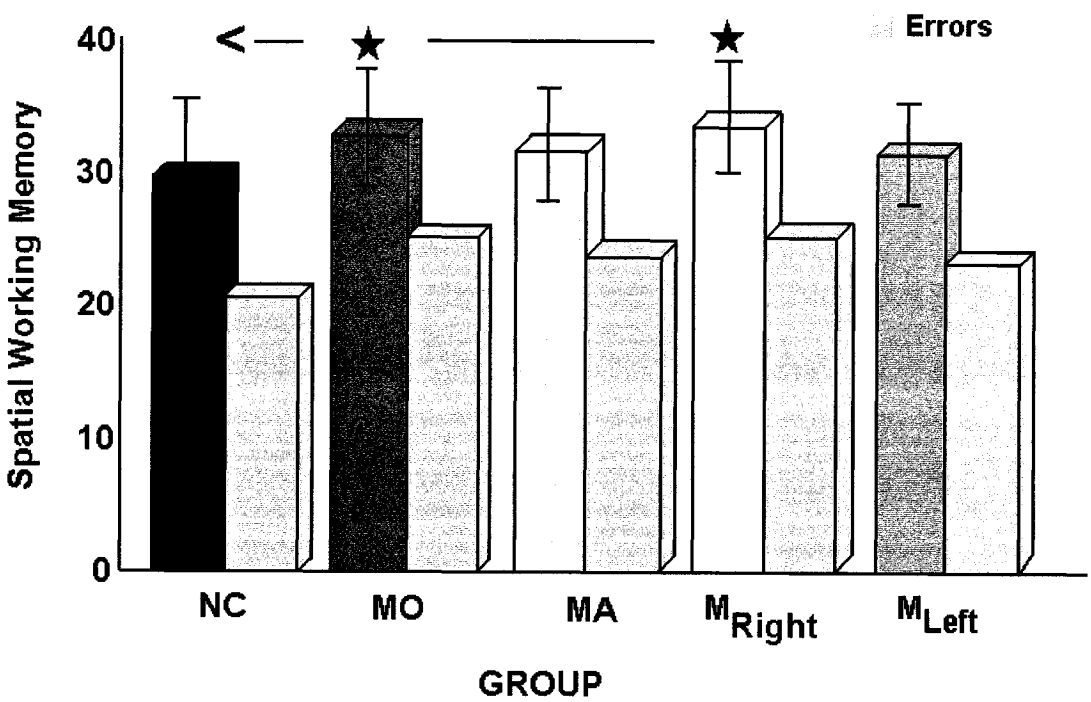
Note. [1]SWM-Strategy = Use of strategy to complete the CANTAB Spatial Working Memory subtest; SOC STT (sec) = the time taken to complete the CANTAB Tower of London subtest after the initial move was made.

[2]df= 4, 34.

[3]df= 2, 36.

*p< .05.

Figure 5. Use of Strategy and Number of Errors on Spatial Working Memory


Errors
40
30
20
10
0
Spatial Working Memory
NC
MO
MA
M Right
M Left
GROUP

Motor Abilities

Motor abilities were assessed using three tests: Tapping, Grooved Pegboard, and Pinch Strength. In general, asymmetries on motor tasks are attributed to the relative proficiency of the contralateral cerebral hemisphere to complete perceptual-motor operations (Todor & Smiley, 1985). To eliminate the possibility of gender differences, results for the motor tasks were analyzed only for the female subjects. ANOVA results are presented in Table 16 and Table S-8. Group differences were found on several tasks including sequential tapping performed with the left hand, right hand performance on the Grooved Pegboard test, and pinch strength bilaterally (Table 17). On the sequential tapping task using the left hand, normal control subjects ($\underline{M}$ = 122.17, $\underline{SD}$ = 7.89) were significantly faster than the M_{Right} patients ($\underline{M}$ = 105.33, $\underline{SD}$ = 14.08). A right-brain advantage has previously been demonstrated in the execution of sequential-spatial tasks and in movement preparation of goal-directed actions (Barthelemy & Boulinguez, 2001; Galluscio, 1983). The poorer left hand sequential tapping performance by M_{Right} patients might reflect a dampening of right hemisphere motor function (Figure 6). On the Grooved Pegboard test, the normal control subjects ($\underline{M}$ = 56.08, $\underline{SD}$ = 6.20) performed significantly faster with the right hand than did the M_{Right} patients ($\underline{M}$ = 65.83, $\underline{SD}$ = 7.28). This performance suggests that M_{Right} may be associated with ipsilateral motor slowness. The normal control subjects had significantly stronger finger pinch strength for both hands (Right Hand: $\underline{M}$ = 17.28, $\underline{SD}$ = 3.16; Left Hand: $\underline{M}$ = 17.28, $\underline{SD}$ = 2.70) than the MA (Right Hand: $\underline{M}$ = 15.07, $\underline{SD}$ = 3.45; Left Hand: $\underline{M}$ = 14.77, $\underline{SD}$ = 3.30) patients.

Table 16

Motor Skills: ANOVA Results

Variable	df	SS	MS	F	p	Power
Sequential Tapping Left Hand						
Group	4	1521.90	380.48	2.32	0.083	0.59
Hemisphere	2	1184.90	592.45	3.61	0.041*	0.62
Type	2	769.92	384.96	2.34	0.115	0.43
Grooved Pegboard Right Hand						
Group	4	550.64	137.66	2.57	0.061	0.64
Hemisphere	2	396.82	198.41	3.70	0.038*	0.63
Type	2	248.42	124.21	2.32	0.118	0.43
Pinch Strength Left Hand						
Group	4	81.92	20.48	2.17	0.100	0.56
Hemisphere	2	54.23	27.12	2.87	0.074	0.52
Type	2	77.08	38.54	4.08	0.028*	0.68
Pinch Strength Right Hand						
Group	4	58.37	14.59	1.97	0.128	0.52
Hemisphere	2	44.13	22.07	2.98	0.068	0.53
Type	2	52.48	26.24	3.54	0.043*	0.61

Note. *$p < .05$.

Table 17

Motor Function: Post-hoc Contrast Tests

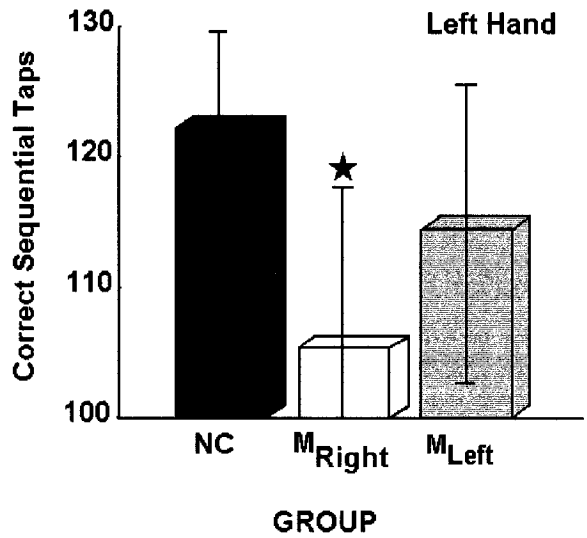
Variable	Contrast	Contrast Value[2]	Std. Error	t	p
STapping-Left Hand[1]					
	NC vs. M_{Right}	16.83	6.09	2.76	0.010**
	NC vs. M_{Left}	7.71	6.40	1.20	0.238
	M_{Right} vs. M_{Left}	-9.12	5.00	-1.82	0.079
Grooved Pegboard Right Hand					
	NC vs. M_{Right}	-9.75	3.51	-2.78	0.010**
	NC vs. M_{Left}	-4.14	3.69	-1.12	0.271
	M_{Right} vs. M_{Left}	5.61	2.89	1.94	0.062
Pinch Strength-Left Hand					
	NC vs. MO	2.27	1.44	1.57	0.126
	NC vs. MA	4.39	1.55	2.83	0.008**
	MO vs. MA	2.13	1.21	1.75	0.090
Pinch Strength-Right Hand					
	NC vs. MO	2.05	1.27	1.61	0.118
	NC vs. MA	3.79	1.37	2.77	0.010**
	MO vs. MA	1.74	1.07	1.64	0.113

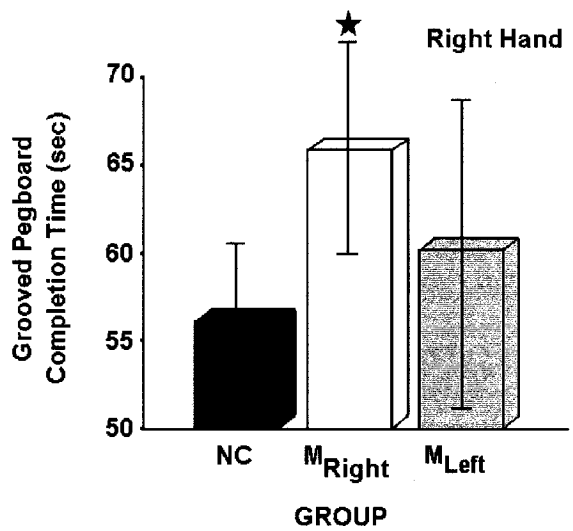
Note. [1]STapping-Left Hand = Sequential tapping executed with the left hand.

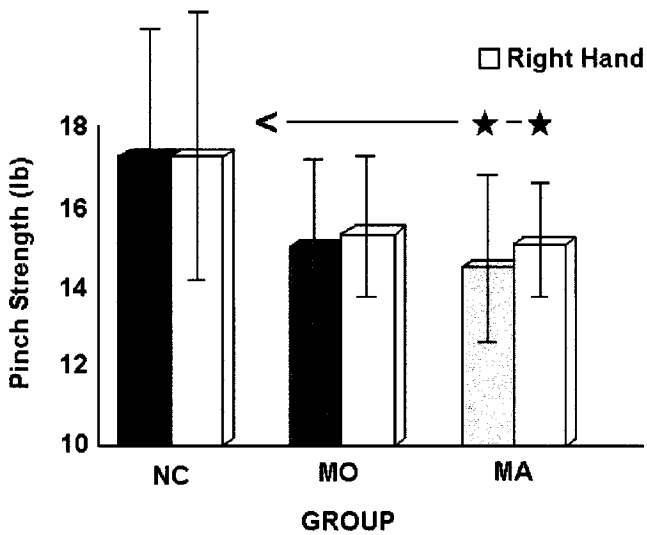
[2]df= 2, 36.

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

Figure 6. Motor Tests Results for Normal Control Subjects and Migraine Patients


Left Hand
Correct Sequential Taps
130
120
110
100
NC
M Right
M Left
GROUP


Right Hand
Grooved Pegboard Completion Time (sec)
70
65
60
55
50
NC
M Right
M Left
GROUP


Right Hand
Pinch Strength (lb)
18
16
14
12
10
NC
MO
MA
GROUP

Statistical Analyses of Composite Neuropsychological Indices

A second statistical approach to the analysis of the neuropsychological data in this study used the Rohling's Interpretative Method (RIM), which groups neuropsychological variables into cognitive domains (Miller & Rohling, 2001). Based on previously published data, every T score was assigned to a specific cognitive domain (Larrabee, Kane, & Schuck 1983; Leonberger, Nicks, Larrabee, & Goldfader, 1992; Lezak, 1995; Nicks, Leonberger, Munz, & Goldfader, 1992; Robertson, Ward, Ridgeway, & Nimmo-Smith, 1996; Shute & Huertas, 1990; Spreen & Strauss, 1998). To obtain a common metric, all test results were transformed into T scores with a mean of 50 and a standard deviation of 10 (Miller & Rohling, 2001). After obtaining a Z score by dividing the results in each subject group by their standard deviation, each Z score was converted to a standardized T score. Standard T scores were obtained by multiplying Z scores with an arbitrary standard deviation of 10 and adding an arbitrary mean of 50. Finally, where appropriate, T scores were transformed such that a lower score would indicate poorer performance. Function composite scores were derived by averaging all the T scores from a cognitive domain, thus giving each test equal weight within its domain as recommended by Miller & Rohling (2001). ANOVAs were conducted to evaluate group differences on the cognitive composite indices (Ernst, Warner, Hochberg, & Townes, 1988; Francis, Fletcher, Rourke, & York, 1992; Larrabee & Curtis, 1995).

Appendix T presents means and standard deviations for the composite psychological measures and non-significant ANOVA results for the working memory,

verbal memory, verbal expression, and emotion and personality composite indices (Table T-1 and Table T-2). Significant group differences were present for the General Cognitive Index, attention and concentration, visuospatial memory, construction abilities, executive function, and motor function indices (Table 18 and Table 19). Taken together, these differences emphasize the presence of relative cognitive difficulties associated with a diagnosis of migraine with aura as well as with migraine pain over the right cerebral hemisphere.

For the General Cognitive Index, normal control subjects ($\underline{M}$ = 52.54, $\underline{SD}$ = 4.37) obtained significantly higher scores than the MA ($\underline{M}$ = 48.56, $\underline{SD}$ = 3.71) and M_{Right} ($\underline{M}$ = 47.69, $\underline{SD}$ = 3.60) patients, and the M_{Left} ($\underline{M}$ = 50.63, $\underline{SD}$ = 4.13) patients obtained significantly higher scores than the M_{Right} patients. Figure 7 presents an illustration of the group results for the General Cognitive Index.

The normal control subjects ($\underline{M}$ = 52.76, $\underline{SD}$ = 6.38) and the M_{Left} patients ($\underline{M}$ = 51.01, $\underline{SD}$ = 5.68) had significantly better attention abilities than did the M_{Right} patients ($\underline{M}$ = 47.66, $\underline{SD}$ = 4.40) as reflected by the results on the attention and concentration index. This pattern of results is comparable to that observed for the performance associated with General Cognitive Index.

Visuospatial memory performance was associated with significantly poorer overall recall for M_{Right} ($\underline{M}$ = 47.35, $\underline{SD}$ = 4.80) than the normal control subjects ($\underline{M}$ = 52.42, $\underline{SD}$ = 5.76) and M_{Left} ($\underline{M}$ = 51.73, $\underline{SD}$ = 5.39). Normal control subjects ($\underline{M}$ =

52.46, SD = 7.80) obtained significantly higher scores on the construction ability index than the M_{Right} patients (M = 47.22, SD = 6.29).

Performance on the executive function composite index, revealed that the normal control subjects (M = 52.01, SD = 3.74) obtained significantly higher scores than MO (M = 47.86, SD = 4.68) and M_{Right} (M = 48.23, SD = 3.52) patients, and the MA patients (M = 51.35, SD = 4.11) obtained significantly higher scores than the MO patients.

Table 18

Cognitive Composite Scores: ANOVA Results

Composite Index	df	SS	MS	F	p	Power
General Cognitive Index						
Group	4	175.70	43.92	2.72	0.046*	0.69
Hemisphere	2	169.56	84.78	5.25	0.010***	0.80
Type	2	85.11	42.55	2.63	0.086	0.49
Attention & Concentration						
Group	4	334.63	83.66	3.24	0.023*	0.77
Hemisphere	2	204.40	102.20	3.96	0.028*	0.67
Type	2	142.44	71.22	2.76	0.077	0.51
Visuo-Spatial Memory						
Group	4	227.74	56.93	1.99	0.118	0.54
Hemisphere	2	224.71	112.36	3.92	0.029*	0.67
Type	2	61.60	30.80	1.08	0.352	0.22
Constructional Abilities						
Group	4	413.38	103.35	3.09	0.028*	0.75
Hemisphere	2	292.51	146.25	4.38	0.020*	0.72
Type	2	94.28	47.14	1.41	0.258	0.28
Executive Function						
Group	4	190.82	47.71	2.65	0.050*	0.68
Hemisphere	2	92.71	46.36	2.58	0.091	0.48
Type	2	134.17	67.09	3.73	0.034*	0.64

Note. *p< .05; ***p<0 .001.

Table 19

Cognitive Composite Scores: Post-hoc Contrast Tests

Variable[1]	Contrast	Contrast Value	Std. Error	t	p
GCI	NC vs. MO	6.45[2]	3.22	2.00	0.053
	NC vs. MA	7.19	3.46	2.07	0.046*
	NC vs. M_{Right}	10.01	3.22	3.11	0.004**
	NC vs. M_{Left}	3.63	3.46	1.05	0.302
	M_{Right} vs. M_{Left}	-6.38	3.08	-2.07	0.046*
	MO vs. MA	0.73	3.08	0.24	0.813
Att & Conc	NC vs. MO	9.22[2]	4.07	2.26	0.030*
	NC vs. MA	3.51	4.38	0.80	0.429
	NC vs. M_{Right}	10.42	4.07	2.56	0.015*
	NC vs. M_{Left}	2.31	4.38	0.53	0.602
	M_{Right} vs. M_{Left}	-8.12	3.89	-2.09	0.044*
	MO vs. MA	-5.72	3.89	-1.47	0.151
VS-Memory	NC vs. M_{Right}	5.07[3]	2.09	2.43	0.020*
	NC vs. M_{Left}	0.69	2.24	0.31	0.760
	M_{Right} vs. M_{Left}	-4.38	1.97	-2.22	0.033*
Constr	NC vs. MO	4.05[2]	4.64	0.87	0.388
	NC vs. MA	8.35	4.98	1.68	0.103
	NC vs. M_{Right}	11.60	4.64	2.50	0.017*
	NC vs. M_{Left}	0.80	4.98	0.16	0.873
	M_{Right} vs. M_{Left}	-10.80	4.42	-2.44	0.020*
	MO vs. MA	4.30	4.42	0.97	0.338
ExecFct	NC vs. MO	7.95[2]	3.40	2.34	0.025*
	NC vs. MA	0.74	3.66	0.20	0.841
	NC vs. M_{Right}	7.05	3.40	2.07	0.046*
	NC vs. M_{Left}	1.64	3.66	0.45	0.657
	M_{Right} vs. M_{Left}	-5.42	3.25	-1.67	0.104
	MO vs. MA	-7.21	3.25	-2.22	0.033*

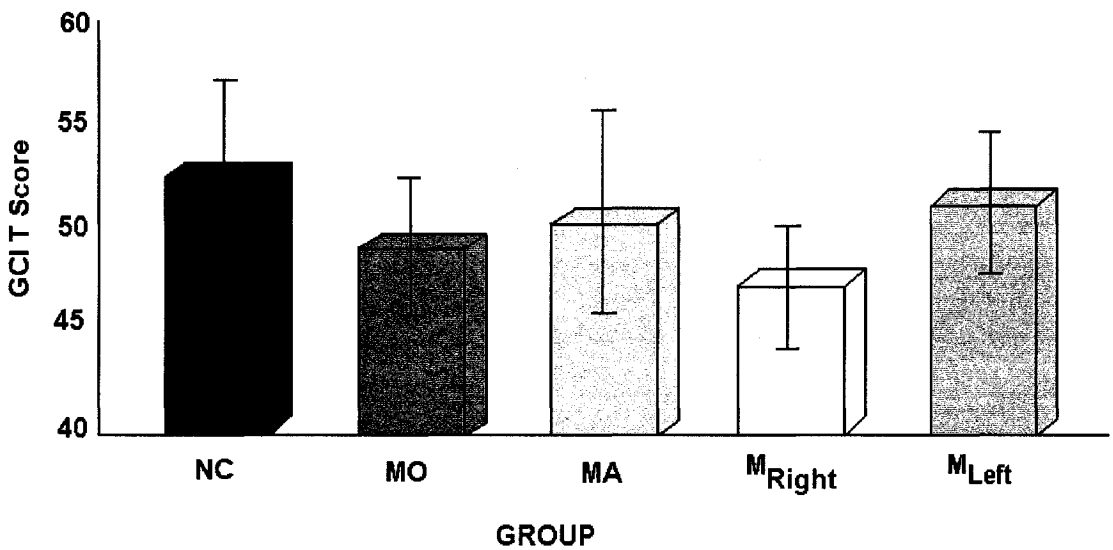
Note. [1]GCI = General Cognitive Index; Att & Conc = Attention and Concentration; VS-Memory = Visuo-Spatial Memory; Constr = Constructional Abilities; ExecFct = Executive Function; Motor-LH = Motor Function of the Left Hand.

[2]df= 4, 34.

[3]df= 2, 36.

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

Figure 7. General Cognitive Index Group Results


60
55
50
45
40
GCI T Score
NC
MO
MA
M Right
M Left
GROUP

DISCUSSION

This dissertation examined two theoretically salient contributors to personality and neuropsychological functioning in migraine patients: the presence or absence of aura, and the hemispheric localization of migraine headache pain. With regard to personality characteristics, we found interesting differences between patients with migraine and normal control subjects. Differences in neuropsychological performance between migraine patients and headache-free subjects were clearly demonstrated. Migraine with aura presents significantly lower scores on measures of cognitive ability than migraine without aura. The impact of the migraine hemispheric location on neuropsychological performance resulted in distinct cognitive profiles for patients with left versus right hemisphere migraines. Finally, we discuss our findings in light of the spreading depression hypothesis and we evaluate whether our data are consistent with the possibility that cerebral right hemisphere and white matter disturbances could account for the impact of migraine hemispheric lateralization on neuropsychological performance.

Personality Profiles

Previous reports have documented increased anxiety, dysphoria, and higher rate of depressive symptoms in patients diagnosed with migraine (Devlen, 1994; Garvey, Tollefson, & Schaffer, 1984; Jarman, Fernandez, Davies, Glover, Steiner, Thompson, Rose, & Sandler, 1990). Selection criteria along with analyses of the scores on the Beck Depression and State Trait Anxiety Inventories ensured that the migraine patients and

normal control subjects did not experience anxiety or depression at the time of testing. Therefore, it is interesting that although the migraine patients and normal control subjects presented comparable anxiety and depression levels at the time of neuropsychological testing, they differed in their personality profiles.

We documented higher levels of self-consciousness and feelings of vulnerability in migraine with aura and left-hemisphere migraine suggesting that these patients may have a stronger emotional reaction to distressing circumstances. It is interesting to note that Hardebo (1991) proposed that hypothalamus disturbances in migraine aura could be responsible for changes in mood states and diminished emotional reactivity. The interpretation of our findings, however, does not coincide with Hardebo's hypothesis but is in agreement with research reporting higher levels of stress susceptibility or neuroticism in patients with migraine than control groups (Mattsson & Ekselius, 2002; Passchier et al., 1988; Persson, 1997). Although autonomic nervous system deficits cannot be fully discounted, we believe that over time patients develop a tendency to overreact to negative situations that is consistent with the chronic, unpredictable nature of their migraine attacks and this tendency is increased in migraine with aura and left-hemisphere migraine. However, given that migraine without aura and right-hemisphere migraine patients presented calm, even-tempered, and confident personality profiles, a diagnosis of migraine does not provide an automatic indicator of emotional difficulties. Based on research supporting a left-hemisphere dysfunction in patients with anxiety and social phobia, we speculate that interference with the processing of verbal input in the left hemisphere could compound the stress levels of patients with left-hemisphere migraine

(Bruder, Schneier, Stewart, McGrath, et al., 2004; Heller, Etienne, & Miller, 1995; Keller, Nitschke, Bhargava, Deldin, et al., 2000; Liotti, Sava, Rizzolatti, & Caffarra, 1991). We found additional personality differences wherein the normal control subjects presented responses associated with imaginative, original personalities while the migraine patients' responses indicated a preference for conventional, conservative response styles. Previously, D'Andrea et al. (1989) reported that children diagnosed with migraine had an increased ability to inhibit aggressive responses as compared to healthy control children. Our data indicate that by adopting predictable or conservative response styles migraine patients may over-regulate their emotions and this augments their ability to cope with unanticipated events including migraine attacks. Thus, further examination of the correlations between personality traits and migraine will be required to ascertain their usefulness in the development of optimal treatment strategies and understanding the underlying mechanisms.

Migraine and Cognitive Abilities

This investigation outlines significant differences in the neuropsychological performance of migraine patients relative to normal control subjects. The average cognitive results for the groups do not represent scores that would be considered below normal limits and it is unknown to what extent they may interfere with everyday life. We also note that the migraine patients participating in this study performed as well as the normal control subjects on many tests (e.g., verbal memory; working memory; attention

and concentration; verbal fluency; executive function) and therefore our findings suggest specific rather than overall effects.

Migraine with Aura and Cognitive Abilities

Several studies found that patients with migraine have cognitive difficulties and motor slowing when compared to normal control groups, and in particular, migraine with aura was associated with greater differences in cognitive abilities than migraine without aura (Kruit et al., 2004; Mulder et al., 1999; Van der Kamp et al., 1996). Consequently, it has been proposed that migraine with aura presents a more profound medical condition (Hooker & Raskin, 1986). Our results show that migraine with aura patients demonstrate reduced cognitive ability on Full Scale and Verbal IQ Ratings, and a General Cognitive Index, as compared to both healthy control subjects and migraine without aura patients. It is interesting to note, however, that in our group migraine with aura patients had a longer spatial span than migraine without aura patients or the normal control subjects, and this finding is in line with Wray et al.'s 1995 report that migraine with aura patients present a reaction-time advantage on simple, but not complex visual detection paradigms. Findings of reduced cognitive abilities in migraine with aura should be further investigated using a longitudinal paradigm that would allow determination of whether there is a progressive deterioration of cognitive function over time.

Cortical Spreading Depression

To explain the etiology of migraine, the cortical spreading depression theory relies upon human and animal demonstrations of neuronal initiation of spreading depression. Of course, in this study, the cortical spreading depression event was not present at the time of testing, but it has been hypothesized that this event, which occurs repetitively in the brain, could lead to long-term interference with normal cognitive abilities (Hadjikhani et al., 2001; Leâo, 1944). Cortical spreading depression is defined as a regenerative process associated with neuronal depolarization that follows an intense excitation of the primary visual cortex. The neuronal depolarization progresses anteriorly towards the parietal and temporal brain areas at a rate of about 2-3 mm/min.

The cortical spreading depression theory proposes that migraine with aura presents a higher susceptibility than migraine without aura for spontaneous neuronal depolarization followed by suppression of cortical function. Behaviourally, the suppression of cortical function is thought to translate into a larger interference with normal cognitive performance. Based on findings of poor ability to process complex visual stimuli, Wray et al. (1995) argued that migraine aura could be explained either by a selective damage of the inhibitory circuits of the primary visual cortex or by increased cortical hyperexcitability. Our data do not exclude a possible deregulation of inhibitory mechanisms in the visual cortex in migraine with aura; however, we suggest that increased cortical excitability could account for the migraine with aura patients' facility to process simple visuo-spatial information as well as their reduced overall cognitive

abilities. The notion of cortical hyperexcitability in migraine aura is also supported by studies using transcranial magnetic stimulation (Aurora et al., 1999; Aurora & Welch, 2000; Van der Kamp et al., 1996) and is consistent with the theory that cortical spreading depression represents the underlying mechanism of migraine.

Another explanation of the observed cognitive discrepancies between migraine with- and without aura is based on the hypothesis that spreading depression is elicited not only by neuronal but also by vascular events. Thus, it is possible that different cognitive profiles are associated with migraine with- and without aura if they are initiated by separate triggering events. Dreier, Kleeberg, Petzold, Priller, et al. (2002) used animal data to demonstrate that spreading depression can be elicited by vascular events, but unequivocal determination from human studies is not yet available. Our data support greater interference with cognitive function associated with migraine with aura, but we cannot conclude whether this interference is the result of different activation mechanisms for migraine with- and without aura.

Migraine Hemisphere Lateralization and Cognitive Abilities

The selection of patients with hemicranial migraine allowed us to examine the relationship between hemispheric location of migraine and cognitive performance. Our control subjects obtained higher scores than either left- or right hemisphere migraine patients on measures of overall cognitive abilities including Full Scale IQ, Verbal IQ, and the derived General Cognitive Index. These results clearly demonstrate a negative

impact of migraine on overall levels of cognitive ability. It is of particular interest that the hemispheric laterality of migraine was associated with separate response patterns: left-hemisphere migraine correlated with significantly reduced Verbal IQ ratings but Performance IQ ratings equivalent to normal control subjects, while right-hemisphere migraine was associated with lower scores on both Verbal and Performance IQ ratings. It is important to note that despite slightly higher Performance IQ ratings, the discrepancy between Verbal and Performance IQ ratings was significantly different in left-hemisphere migraine as compared to normal control subjects. This finding strongly suggests that while migraine with left hemisphere focus has a negative impact on verbal performance, visuo-spatial abilities remain unaltered.

The significantly lower scores of the of the patients with right-hemisphere migraine on tasks of visuo-spatial memory, attention and concentration, constructional abilities (i.e., manipulation of three-dimensional blocks and copying of a complex figure), executive function, and motor skills suggest possible interference with the function of the right hemisphere. A large body of evidence from lesion studies supports a right hemisphere advantage for attending to, processing, and storing visuo-spatial relations (Barthelemy & Boulinguez 2001; Gazzaniga et al., 1965; Kolb & Whishaw, 2003; Milner & Taylor, 1972; Stuss, Binns, Murphy, & Alexander, 2002). Similarly, constructional skills such as the ability to build three-dimensional blocks into specific patterns and to draw a picture from a model rely on adequate visuo-spatial abilities and motor execution and are sensitive to right hemisphere damage, most commonly in posterior parietal areas (Black & Strub, 1976; Farah, 2003; Heilman et al., 2003;

Newcombe, 1969; Reitan, 1986). Recently, Le Pira et al. (2004) reported that right-hemisphere migraine was correlated with diminished performance on visuo-spatial memory and semantic clustering tasks for concrete words, and took these data to indicate right hemisphere dysfunction in patients with migraine. We note that previous evidence is available with regard to a right hemisphere advantage for processing high imagery or concrete words (Villardita, 1987; Villardita, Grioli, & Quattropani, 1988).

Our findings support a right hemisphere disadvantage in patients with right-hemisphere migraine but it is also possible that, consistent with the cortical spreading depression hypothesis, they are the consequence of white matter changes. In light of research pointing to white matter disturbances in migraine, the demonstration of reduced left hand motor performance in the right-hemisphere migraine in our study provides provisional behavioural support for this hypothesis (Kruit, Launer, van Buchem, Terwindt, et al., 2005; Porter, Gladstone, & Doddick, 2005; Scherer et al., 1997). Kruit et al. (2004) found that Multiple Sclerosis patients with known white matter lesions performed in a similar manner to migraine patients on a finger-tapping test and concluded that patients with migraine might present slight structural abnormalities in cerebral white matter.

Another possible explanation of results associated with right-hemisphere migraine is that this diagnosis may be consistent with the development of a non-verbal learning disabilities like condition. Rourke, Ahmad, Collins, Hayman-Abello, et al. (2002) have reviewed this childhood syndrome and proposed that a 'non-developmental' NLD can be

diagnosed in adolescents and adults subsequent to right hemisphere damage or neurological disorders with documented white matter dysfunction. The general diagnostic criteria for non-verbal learning disabilities include difficulties in the areas of visuo-spatial memory, concept formation, hypothesis testing, problem solving, and execution of complex motor skills. This syndrome complex is remarkably similar to the one seen in the present investigation in the patients with right hemisphere migraine in whom we observed executive function difficulties related to efficient strategy allocation. These difficulties are compatible with observations of concept formation deficits and inappropriate use of strategy among patients with right-sided lesions and imaging data showing right hemisphere activation during tasks that rely on switching of acquired attentional biases to new stimuli (Miotto, Bullock, Polkey, & Morris, 1996; Rogers, Andrews, Grasby, Brooks, et al., 2000).

Concluding Remarks

Despite similar cognitive abilities on several tasks, this investigation demonstrates specific cognitive differences in migraine patients as compared to normal control subjects. Our findings support previous work indicating that migraine with aura represents a more severe neurological disturbance than migraine without aura. We ascertained that the hemispheric location of migraine plays a key role in determining the pattern of cognitive difficulties associated with this disorder such that left hemisphere migraines are associated with lower scores on verbal tasks while right hemisphere migraines demonstrate difficulties on both verbal and visuo-spatial tasks. This

investigation established right-hemisphere migraine as having a more profound effect on cognition. The present study could not provide direct evidence for the applicability of the cortical spreading depression theory to migraine with and without aura, therefore additional data will be needed to verify the impact of neuronal and vascular triggers on spreading depression and assess their differential impact on specific forms of migraine.

This research could not ascertain whether migraine may be associated with a progressive deterioration of cognitive function. Consequently, the application of a longitudinal paradigm could elucidate the long-term impact of migraine with and without aura on neuropsychological abilities. In addition, because of the relatively small patient sample used in the present investigation, larger groups will be needed to confirm the current findings and further characterize the cognitive profile of migraine patients. Combining investigative tools such as neuro-imaging and behavioural instruments will be necessary to elucidate the etiology of this complex neurological disorder and confirm whether the distinct cognitive profiles associated with the hemispheric laterality of migraine can be correlated with underlying anatomical changes.

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APPENDIX A

Studies of Cognitive Function in Migraine Patients: Test Batteries

Studies of Cognitive Function in Migraine

Neuropsychological tests assessing cognitive abilities of migraine patients

Migraine and Impaired Cognitive Performance

Calandre, Bembibre, Arnedo, & Becerra (2002)

WAIS
Stroop Test
Strub and Black Letter Test
Trail Making Test
Rey Auditory Verbal Learning Test
WMS (Logical Memory and Visual Reproduction subtests)
Rey-Osterrieth Complex Figure
Benton Visual Retention
Benton Facial Recognition
Luria Sequential Motor Tasks
Rapid Alternating Hand Movements
Rhythm Test
Poppelrenter Test
Beck Depression Inventory
Taylor Manifest Anxiety Scale

Conlon & Humphreys (2000)

Visual Discomfort
Automatic (Parallel Search) Attention Task
Conscious (Serial Search) Attention Task

D'Andrea et al. (1989)

Raven's Coloured Progressive Matrices
Digit Span
Rey Complex Figure
Logical Memory Test
Ten Word Learning Test
Human Figure Test
Test of the Tree
Picture Frustration Study
Anxiety Questionnaire

Hooker & Raskin (1986)

Wechsler Adult Intelligence Scale Revised
Digit Span
Block Design
Digit Symbol
Similarities
Wechsler Memory Scale–Russell Revision
Aphasia Screening Test
Raven Progressive Matrices
Trail Making Test
Wisconsin Card Sorting Test
Smedley Hand Dynamometer Test
Grooved Pegboard Test
Finger Tapping Test
Tactual Performance Test
Sensory Perceptual Composite Score

Le Pira, Zappala, Giuffrida, Lo Bartolo, Reggio, Morana, & Lanaia (2000)

Boston Scanning Test
Raven Progress Matrices '47
Verbal Fluency Task
Rey Complex Figure
Digit Span
Corsi Block Tapping
California Verbal Learning Test

Mulder, Linssen, Passchier, Orlebeke, de Geus (1999)

The Neurobehavioural Evaluation System:
Verbal Reasoning
Simple Reaction Time
Switching of Attention
Finger Tapping
Hand-Eye Coordination Task
Continuous Performance with Pictures and Letters
Stroop Test
Serial Digits
Symbol Digit Substitution
Horizontal Addition
Visual Digit Span
Pattern Comparison
Pattern Memory

Palmer & Chronicle (1998)

Word Priming Task
Orientation Search
Temporal discrimination task

Waldie, Hausmann, Milne, & Poulton (2002)

Age 3: Peabody Picture Vocabulary Test
Age 7: Handedness Test
Ages 7 & 9: Illinois Test of Psycholinguistic Ability (Verbal Comprehension and Verbal Expression subscales)
Ages 7, 9, 11, & 13: WISC-R (excluding the Comprehension and Picture Arrangement subscales)
Ages 7, 9, 11, 13, 15, & 18: Burt Reading Test
Age 11: Pure Tone Threshold Determination
Ages 11 & 13: Speech-in-Noise Test

Wray, Mijovic-Prelec, & Kosslyn (1995)

Low-level Visual Paradigm
    Orientation Detection Task
    Temporal Order Judgment Test

High-level Visual Processing
    Picture Naming Test
    Word Priming Task

Zeitlin & Oddy (1984).

Stroop Colour/Word Test
Trail Making Test
Choice Reaction Time
Paced Auditory Serial Addition Test
National Hospital Forced Choice Recognition Test (words and faces)
Mill Hill Vocabulary Scale
Middlesex Hospital Questionnaire

Migraine and standard cognitive performance

Leijdekkers et al. (1990)

Groninger Intelligence Test
WAIS-R
Block Design
Digit Symbol
Letter-Series Test
Neurobehavioural Evaluation System
Measure of Invested Mental Effort
State Trait Anxiety Inventory
Achievement Motivation Test

Bell et al. (1999)

Logical Memory
Verbal Paired Associates
Visual Reproduction (WAIS-R)
Controlled Oral Word Association Test
Paced Auditory Serial Addition Test
The Beck Depression Inventory
Pain symptoms Questionnaire

Jelic, van Boxtel, Houx, & Jolles (2000)

Letter Digit Substitution
Verbal Learning Test

Meyer, Thornby, Crawford, & Rauch (2000)

Mini-Mental Status Examination
Cognitive Capacity Screening Examination
Hamilton Depression Rating Scale

Sinforiani et al. (1987)

Tachistoscopic tasks

APPENDIX B

Initial Recruitment by Neurologist: Patient Selection Sheets

PATIENT SELECTION SHEET

EVALUATION OF NEUROPSYCHOPHYSIOLOGICAL FUNCTION IN

MIGRAINE PATIENTS WITH AND WITHOUT AURA

Investigators: D. Milovan, G. Leonard, M. Aubé, & L. Durcan

Patient NAME:
DOB: _____
DATE (INFO GATHERED): _____

Inclusion Criteria		
Unilateral migraine	Left-Sided	
	Right-Sided	
	With aura	
	Without aura	
# Migraine/month		
Patient Info		
Substance abuse	Opiate analgesics	
	Psychotropic drugs	
	Ergotamine	
	Medication specific for migraine	
	Alcohol	
Systemic and/or CNS disease		
Learning disability		
History of psychiatric illness		
Use of prophylactic (preventive) medication		
Family history of epilepsy		
Notes		

PATIENT SELECTION CRITERIA

Patient NAME:

Inclusion Criteria

Unilateral migraine: Left-Sided: _____ Right-Sided: _____

Migraine with aura _____ Migraine without aura _____

No less than 2 migraines per month / **no more than 4** migraines per month.
migraines per month: _____

Exclusion Criteria

Current or past (less than 6 months) history of substance abuse: opiate analgesics (i.e., medication that can modify mood and has a potential for abuse), psychotropic drugs (i.e., drugs that have an effect on psychological function like antidepressants, anti-anxiety drugs, drugs that control hallucinations), ergotamine (>10 mg/week; medication specific for migraine), alcohol: (> 315 g/week) Yes ___ No ___

Systemic and/or CNS disease (e.g., epilepsy, head injury) Yes ___ No ___

History of learning disability Yes ___ No ___

History of psychiatric illness (e.g., major depression, generalized anxiety disorder) Yes ___ No ___

Use of prophylactic (preventive) medication: MAO inhibitors, beta-blockers, Serotonin reuptake inhibitors, Lithium. Yes ___ No ___

Describe: _____
_____

Family history of epilepsy Yes ___ No ___

APPENDIX C

Consent Forms

– English and French Versions –

EVALUATION OF NEUROPSYCHOLOGICAL FUNCTION IN MIGRAINE PATIENTS WITH AND WITHOUT AURA

CONSENT FORM

MONTREAL NEUROLOGICAL INSTITUTE & HOSPITAL

Title of Project: Evaluation of neuropsychological function in migraine patients with and without aura.

Investigators: D. Milovan, G. Leonard, M. Aubé, & L. Durcan

REASON FOR THE STUDY

This study will investigate whether differences in brain structure and function are present between patients diagnosed as having migraine and healthy subjects. We will first administer a number of different psychological tests in order to obtain a careful documentation of your level of general cognitive function. In addition, you will be asked to complete several questionnaires that look at personality characteristics and your emotional well-being.

PROCEDURES

After an interview with a doctor, we will bring you back several times to do the following tests: (1) neuropsychological tests and questionnaires about your emotional well being (three hours) and (2) take-home questionnaire examining personality traits (one hour).

Neuropsychological tests

These tasks will take one session of approximately three hours to complete.

During the session, we will ask you to perform different tasks such as to draw pictures, name objects, remember stories, etc. You will also be required to fill out questionnaires about your mood.

Take-Home Questionnaires

There will be one take-home questionnaire to be filled out and returned to the investigators within one week. This questionnaire pertains to personality traits and will take about one hour to complete.

3. CONTRAINDICATION

There are no contraindications for these Neuropsychological Tests and Questionnaires.

4. ADVANTAGES OF THE PROPOSED STUDIES

It is hoped that the information obtained from the administration the neuropsychological tests and questionnaires will improve our understanding of the functions of the human brain. This, in the long term, may help the diagnosis and treatment of neurological disorders, such as migraine.

5. DISADVANTAGES OF THE PROPOSED STUDIES

None

6. EFFECTS OF PARTICIPATION IN THIS STUDY ON YOUR TREATMENT

Neuropsychological testing does not interfere with any treatment or other diagnostic tests.

7. CONFIDENTIAL NATURE OF THE STUDY

The results of the testing will be kept strictly confidential. No personal information will be released to third parties without your written approval.

8. INCIDENTAL FINDINGS

Any incidental findings regarding your health will be communicated to you or to your physician, at your request.

9. DISCONTINUATION OF THE STUDY BY THE INVESTIGATOR

At any time during the testing, the investigators have the right to terminate the study for any reason.

10. SUBJECT'S STATEMENT CONCERNING WITHDRAWAL FROM THE STUDY

I understand that my participation in this research project is voluntary and I may withdraw at any time, including during the procedure, without prejudice to my treatment or myself.

EVALUATION OF NEUROPSYCHOLOGICAL FUNCTION IN MIGRAINE PATIENTS WITH AND WITHOUT AURA

MONTREAL NEUROLOGICAL INSTITUTE & HOSPITAL
3801 University Street, Montreal, Quebec, Canada, H3A 2B4
D. Milovan, G. Leonard, M. Aubé, & L. Durcan

SUBJECT'S DECLARATION OF CONSENT

I, _____, have read the above description with one of the above investigators, _____.

I fully understand the procedures, advantages, and disadvantages of this study that have been explained to me. I freely and voluntarily consent to participate in this study.

Furthermore, I understand that I may seek information about each test either before or after it is given, that I am free to withdraw from the testing at any time if so I desire, and that my personal information will be kept confidential.

SIGNATURE _____	_____	_____	
	SUBJECT	DATE	CONTACT NO.
SIGNATURE _____	_____	_____	
	INVESTIGATOR	DATE	CONTACT NO.
SIGNATURE _____	_____	_____	
	WITNESS	DATE	CONTACT NO.
SIGNATURE _____	_____	_____	
	PHYSICIAN	DATE	CONTACT NO.

EVALUATION DES FONCTIONS NEUROPSYCHOLOGIQUES CHEZ LES PATIENTS MIGRAINEUX AVEC ET SANS AURA

FORMULAIRE DE CONSENTMENT

INSTITUT ET HÔPITAL NEUROLOGIQUES DE MONTRÉAL

Titre du projet: Évaluation des fonctions neuropsychologiques chez les patients migraineux avec et sans aura.

Chercheurs: D. Milovan, G. Leonard, M. Aubé, & L. Durcan

1. BUT DE L'ÉTUDE

Cette étude aura pour but d'examiner l'existence de différences de structure et de fonction cérébrales entre des patients présentant différents symptômes de migraine et des personnes en bonne santé. Dans un premier temps, nous allons vous faire passer un certain nombre de tests psychologiques dans le but d'arriver à une meilleure compréhension de votre niveau de fonctionnement cognitif général. De plus, nous vous demandons de compléter plusieurs questionnaires portant sur des caractéristiques de personnalité ainsi que sur votre état émotionnel.

2. PROCÉDURES

Après une entrevue initiale avec un médecin, nous allons vous demander de revenir plusieurs fois pour chacune des expériences suivantes : (1) tests neuropsychologiques et questionnaires portant sur votre état émotionnel (trois heures) et (2) un questionnaire à remplir chez vous portant sur des caractéristiques de personnalité (une heure).

Tests neuropsychologiques

Cette expérience durera environ trois heures.

Pendant cette session, on vous demandera de compléter des tâches différentes comme reproduire des dessins, nommer des objets, se souvenir d'histoires, etc. De plus, on va vous demander de compléter des questionnaires portant sur votre bien-être émotionnel.

Questionnaire pour compléter à la maison

Un questionnaire à compléter chez vous vous sera également remis. Ce questionnaire devra être rapporté aux investigateurs avant une semaine. Il porte sur vos croyances personnelles et prendra environ une heure à remplir.

3. CONTRE-INDICATIONS

Il n'y a pas de contre-indication pour cette procédure.

4. AVANTAGES DES ÉTUDES PROPOSÉES

Nous espérons que les renseignements obtenus à partir de l'administration des tests et questionnaires neuropsychologiques nous aideront à mieux comprendre le fonctionnement du cerveau humain. Cela pourra à long terme contribuer au diagnostic et au traitement des troubles neurologiques tel que les migraines.

5. INCONVÉNIENTS DES ÉTUDES PROPOSÉES

Aucun

6. EFFETS DE VOTRE PARTICIPATION À CETTE ÉTUDE SUR VOTRE TRAITEMENT

Les tests neuropsychologiques n'interférèrent pas avec aucun traitement ni examen diagnostique.

7. CARACTÈRE CONFIDENTIEL DE CETTE ÉTUDE

Les résultats des études seront confidentiels. Aucune donnée vous concernant ne sera transmise à un tiers sans votre autorisation écrite.

8. CONSTATATIONS FORTUITES

Toute constatation fortuite concernant votre santé sera portée à votre connaissance ou à celle de votre médecin, si vous en faites demande.

9. INTERRUPTION DE L'ÉTUDE PAR LE CHERCHEUR

Les chercheurs ont le droit de mettre fin à cette étude à tout moment, pour n'importe quel raison.

10. DÉCLARATION DES SUJETS À PROPOS DU DÉSISTEMENT

Il est entendu que ma participation à ce projet est purement volontaire et que je peux m'en désister à tout moment, y compris pendant son déroulement, sans que cela soit préjudiciable à moi-même ou à mon traitement.

EVALUATION DES FONCTIONS NEUROPSYCHOLOGIQUES CHEZ LES PATIENTS MIGRAINEUX AVEC ET SANS AURA INSTITUT ET HÔPITAL NEUROLOGIQUES DE MONTRÉAL

3801 Rue University, Montréal, Québec, Canada, H3A 2B4
D. Milovan, G. Leonard, M. Aubé, & L. Durcan

DÉCLARATION DE CONSENTEMENT DU SUJET

Je soussigné(e) _____ ai pris connaissance de ce qui précède en présence de l'un des chercheurs suivants _____.

J'ai parfaitement compris les procédures, les avantages et les inconvénients de cette étude. Je consens volontairement à y participer. Il est entendu par ailleurs que je peux demander des renseignements à propos de chaque examen avant ou après son déroulement, que je suis libre de me désister de ce protocole à tout moment si je le souhaite et que toute donnée me concernant restera confidentielle.

SIGNATURE _____	_____	_____
SUJET	DATE	NO DE CONTACT
SIGNATURE _____	_____	_____
CHERCHEUR	DATE	NO DE CONTACT
SIGNATURE _____	_____	_____
TÉMOIN	DATE	NO DE CONTACT
SIGNATURE _____	_____	_____
MÉDECIN	DATE	NO DE CONTACT

APPENDIX D

Subject Contact: Study Explanation and Confirmation of Participation

– English and French Versions –

EVALUATION OF NEUROPSYCHOPHYSIOLOGICAL FUNCTION IN INDIVIDUALS WITH MIGRAINES WITH AND WITHOUT AURA

MONTREAL NEUROLOGICAL INSTITUTE & HOSPITAL

Investigators: D. Milovan, G. Leonard, M. Aubé, L., & Durcan

Summary

This study will investigate whether differences in cognitive function and cerebral activity are present between subjects diagnosed as having left or right-sided migraines and subjects who do not experience migraines.

Neuropsychological tests and questionnaires will be administered. The neuropsychological test battery will last for approximately 3½ hours and will include tasks related to attention, short- and long-term memory and motor skills. One of the take-home questionnaires will provide information about your migraine history (e.g., frequency and duration of attacks, associated features such as nausea, vomiting, light, and /or sound aversion, etc). The remaining questionnaires will gather information about the personality characteristics and emotional state (e.g., feelings of anxiety and depression) of people with and without a history of migraines.

Test duration is **between 3 - 4 hours (8:30 am – 11:30 am/12:30 pm).** It is important to tell the subject that the testing may actually take up to 4 hours.
Migraine subjects **should be migraine-free** for a minimum of **2 days before** testing).

(**NOTE.** It **is** possible to have the second day of testing if the patient is too tired to complete everything within one session).

PATIENT SELECTION CRITERIA

Unilateral migraines: Left-Sided: _____ Right-Sided: _____
Migraines with aura _____ Migraines without aura _____
Number of migraines/ Month: _____

Relevant Phone numbers (to give to patient)
Neuropsychology Department: (514) 398-8504
Denise Milovan: (514) 398-8472

EVALUATION DES FONCTIONS NEURO-PSYCHOLOGIQUES CHEZ LES PERSONNES AVEC DES MIGRAINES AVEC OU SANS AURA

INSTITUT ET HÔPITAL NEUROLOGIQUES DE MONTRÉAL

Chercheurs: D. Milovan, G. Leonard, M. Aubé, & L. Durcan

Sommaire

Cette étude consiste à examiner les différences présentes dans les fonctions cognitives et dans l'activité cérébrale entre des personnes présentent des migraines localisées soit du côté droit soit du côté gauche de la tête et des personnes dits "en bonne santé."

Des tests psychologiques (d'une durée d'environ 3½ heures) et une série des questionnaires (à compléter à la maison) vous seront administrés. Les tests psychologiques portent sur l'attention, la mémoire à court et à long terme, ainsi que sur la capacité de contrôler vos mouvements. Les questionnaires comprennent des questions concernant l'histoire de vos migraines (comme par exemple, la fréquence et la durée des migraines, et d'autres caractéristiques associées aux migraines comme la nausée, l'aversion à la lumière, l'aversion aux sons, etc.). De plus, des questions portant sur des caractéristiques émotionnelles et de personnalité vous seront aussi administrées.

La durée des tests est **d'environ 3 – 4 heures (8:30am – 11:30am / 12:30pm).** Il est important de mentionner ceci au sujet.
On conseille que les patients **doivent <u>être sans migraine</u>** pour au moins **2 jours avant** la session de tests.

(**<u>NOTE</u>.** Il **sera** possible de finir les tests plus tard, si le sujet se sent fatigue).

CRITÈRES DE SÉLECTION DES PATIENTS

Migraines Unilatérales: Côté gauche: _____ Côté Droit: _____
Migraines avec aura _____ Migraines sans aura _____
Migraines par mois: _____

Numéros de téléphone à donner au sujet
Neuropsychology Département: (514) 398-8504
Denise Milovan: (514) 398-8472

Patient Information Sheet

(To be included in patient file)

CODE: _____

Name: _____ _____
Last First

Date for Neuropsychological Testing: _____
Month / Day / Year

Date of Last Migraine Attack Prior to Testing: _____
Month / Day / Year

Date of First Migraine Attack after Testing: _____
Month / Day / Year

Patient Phone Number(s): Day: _____
Evening: _____

APPENDIX E

Beck Depression Inventory

– French Version –

TEST DE BECK

Ce questionnaire renferme des groupes d'énoncés. Veuillez lire attentivement chaque énoncé. Par la suite, indiquez l'énoncé de chaque groupe répondant le mieux à comment vous vous êtes senti(e) cette semaine incluant aujourd'hui. Encerclez le chiffre précédant l'énoncé choisi. Si plusieurs énoncés d'un même groupe s'appliquent, encerclez-les. Assurez-vous de lire chaque énoncé avant de faire un choix.

1. 0 Je ne me sens pas triste.
   1 Je me sens triste.
   2 Je suis toujours triste et je ne semble pas pouvoir m'en sortir.
   3 Je suis tellement triste et malheureux(se) que je ne peux pas le supporter.

2. 0 Je ne me sens pas particulièrement découragé(e) face à l'avenir.
   1 Je me sens découragé(e) face à l'avenir.
   2 Je n'attends rien de l'avenir avec anticipation.
   3 J'ai l'impression que l'avenir ne me réserve aucun espoir et que les choses ne peuvent pas s'améliorer.

3. 0 Je n'ai pas l'impression d'être un échec.
   1 Je ai crois avoir échoué plus qu'une personne moyenne.
   2 Quand je regarde ce que j'ai accompli dans ma vie jusqu'ici, je vois beaucoup d'échecs.
   3 J'ai l'impression d'être un échec total.

4. 0 Je retire autant de satisfaction des choses comme je l'ai toujours fait.
   1 Je ne prend pas plaisir aux choses comme avant.
   2 Je ne prend vraiment pas de plaisir à rien.
   3 Je suis mécontent(e) ou ennuyé(e) par tout.

5. 0 Je ne me sens pas particulièrement coupable.
   1 Je me sens coupable une grande partie du temps.
   2 Je me sens coupable la majorité partie du temps.
   3 Je me sens coupable tout le temps.

6. 0 Je n'ai pas l'impression d'être puni.
   1 Je crois peut-être puni(e).
   2 Je m'attends à être puni(e).
   3 J'ai l'impression d'être puni(e).

7. 0 Je ne suis pas déçu(e) de moi.
   1 Je suis déçu(e) de moi.
   2 Je suis dégoûté(e) de moi.
   3 Je me haïs.

8. 0 Je ne crois pas être pire que les autres.
1 Je me critique pour mes faiblesses et mes erreurs.
2 Je me blâme constamment pour mes erreurs.
3 Je me blâme pour tout ce qui va mal.

9. 0 Je n'ai aucune idée de me tuer.
1 Je pense à me tuer mais je ne le ferais pas.
2 J'aimerais me tuer.
3 Je me tuerais si j'avais l'occasion.

10. 0 Je ne pleure pas plus que normalement.
1 Je pleure plus qu'avant.
2 Je pleure tout le temps à présent.
3 Je pouvais pleurer avant mais j'en suis plus capable même si je le veux.

11. 0 Je ne suis pas plus irrité(e) maintenant que je le suis normalement.
1 Je suis contrarié(e) et irrité(e) plus facilement qu'avant.
2 Je suis irrité(e) tout le temps à présent.
3 Je ne suis plus irrité(e) par les choses qui m'irritaient auparavant.

12. 0 Je n'ai pas perdu intérêt pour les autres personnes.
1 Je suis moins intéressé(e) aux autres personnes qu'avant.
2 J'ai perdu beaucoup d'intérêt pour les autres personnes.
3 J'ai perdu tout intérêt pour les autres personnes.

13. 0 Je prends des décisions aussi bien qu'avant.
1 Je remets les prises de décisions plus qu'avant.
2 J'éprouve plus de difficultés à prendre des décisions qu'avant.
3 Je ne peux plus prendre de décisions du tout.

14. 0 Je ne crois pas paraître plus mal qu'avant.
1 Je suis inquiet(éte) de paraître vieux/vieille et peu attrayant(e).
2 Je sens qu'il y a des changements permanents dans mon apparence qui me font paraître peu attrayant(e).
3 Je crois paraître laid(e).

15. 0 Je peux travailler aussi bien qu'avant.
1 Ça prend un certain effort pour que je commence quelque chose.
2 Je dois me pousser très fort afin d'accomplir quelque chose.
3 Je ne peux accomplir rien du tout.

16. 0 Je peux dormir aussi bien qu'avant.
1 Je ne dors pas aussi bien qu'avant.
2 Je me réveille une ou deux heures plus tôt qu'à l'habitude et il m'est difficile de me rendormir.
3 Je me réveille plusieurs heures plus tôt qu'à l'habitude et je ne peux pas me rendormir.

17. 0 Je ne deviens pas plus fatigué(e) qu'à l'habitude.
1 Je deviens plus fatigué(e) qu'avant.
2 Je deviens fatigué(e) en ne faisant presque rien.
3 Je suis trop fatigué(e) pour entreprendre quoi que ce soit.

18. 0 Mon appétit n'est pas pire qu'à l'habitude.
1 Mon appétit n'est pas aussi bon qu'avant.
2 Mon appétit est pire à présent.
3 Je n'ai plus aucun appétit à présent.

19. 0 Je n'ai pas perdu beaucoup de poids récemment. J'essaie de perdre du poids en mangeant moins OUI ____ NON ____
1 J'ai perdu plus de 5 livres
2 J'ai perdu plus de 10 livres
3 J'ai perdu plus de 15 livres

20. 0 Je ne me préoccupe pas plus de ma santé qu'avant.
1 Je m'inquiète de problèmes physiques tells douleur et maux, estomac perturbé ou constipation.
2 Je m'inquiète beaucoup de problèmes physiques et il est difficile de ne pas y penser.
3 Je m'inquiète tellement de problèmes physiques que je ne peux penser à rien d'autre.

21. 0 Je ne me suis pas aperçu(e) d'aucun changement récent dans mon intérêt envers la sexualité.
1 Je suis moins intéressé(e) à la sexualité qu'avant.
2 Je suis beaucoup moins intéressé(e) à la sexualité à présent.
3 J'ai perdu tout intérêt envers la sexualité.

APPENDIX F

Questionnaire d'Évaluation Personnelle: ASTA

– French Version –

QUESTIONNAIRE D'ÉVALUATION PERSONNELLE: ASTA

Adaptation française du questionnaire STAI
(Spielberger, Gorsuch, & Lushene, 1970)
Jacques Bergeron et Michel Landry

CONSIGNE: Voici un certain nombre d'énoncés que les gens ont l'habitude d'utiliser pour se décrire. Lisez chaque énoncé, puis encerclez le chiffre approprié à droite de l'exposé pour indiquer comment vous vous sentez présentement, c'est-à-dire à ce moment précis. Il n'y a pas de bonnes ou mauvaises réponses. Ne vous attardez pas trop sur chaque énoncé mais donnez la réponse qui vous semble décrire le mieux les sentiments que vous éprouvez en ce moment.

	PAS DU TOUT	UN PEU	MODERE-MENT	BEAU-COUP
Je me sens calme.	1	2	3	4
Je me sens en sécurité.	1	2	3	4
Je suis tendu.	1	2	3	4
Je suis triste.	1	2	3	4
Je me sens tranquille.	1	2	3	4
Je me sens bouleversé.	1	2	3	4
Je suis préoccupé actuellement par des contrariétés possibles.	1	2	3	4
Je me sens reposé.	1	2	3	4
Je me sens anxieux.	1	2	3	4
Je me sens à l'aise.	1	2	3	4
Je me sens sûr de moi.	1	2	3	4
Je me sens nerveux.	1	2	3	4
Je suis affolé.	1	2	3	4
Je me sens sur le point d'éclater.	1	2	3	4
Je suis relaxé.	1	2	3	4
Je me sens heureux.	1	2	3	4
Je suis préoccupé.	1	2	3	4
Je me sens surexcité et fébrile.	1	2	3	4
Je me sens joyeux.	1	2	3	4
Je me sens bien.	1	2	3	4

CONSIGNE: Voici un certain nombre d'énoncés que les gens ont l'habitude d'utiliser pour se décrire. Lisez chaque énoncé, puis encerclez le chiffre approprié à droite de l'exposé pour indiquer comment vous vous sentez en général. Il n'y a pas de bonnes ou mauvaises réponses. Ne vous attardez pas trop sur chaque énoncé mais donnez la réponse qui vous semble décrire le mieux les sentiments que vous éprouvez de façon générale.

	Présque Jamais	Quelque Fois	Souvent	Présque Toujours
Je me sens bien	1	2	3	4
Je me fatigue rapidement	1	2	3	4
Je me sens au bord des larmes	1	2	3	4
Je souhaiterais être aussi heureux(se) que les autres semblent l'être	1	2	3	4
Je perds de belles occasions parce que je n'arrive pas à me décider assez rapidement	1	2	3	4
Je me sens repose(e)	1	2	3	4
Je suis calme, tranquille et en paix	1	2	3	4
Je sens que les difficultés s'accumulent au point que je ne peut pas en venir à bout	1	2	3	4
Je m'en fais trop pour les choses qui n'en valent pas vraiment la peine	1	2	3	4
Je suis heureux(se)	1	2	3	4
Je suis porté(e) à prendre mal les choses	1	2	3	4
Je manqué de confiance en moi	1	2	3	4
Je me sens en sécurité	1	2	3	4
J'essaie d'éviter de faire face à une crise ou une difficulté	1	2	3	4
Je me sens mélancolique	1	2	3	4
Je suis content(e)	1	2	3	4
Des idées sans importance me passent par la tête et me tracassent	1	2	3	4
Je prends les désappointements tellement à coeur que je n'arrive pas à les sortir de la tête	1	2	3	4
Je suis une personne stable	1	2	3	4
Je deviens tendu(e) et boulversé(e) quand je songe à mes préoccupations actuelles	1	2	3	4

APPENDIX G

Neuropsychological Test Battery

MIGRAINE TEST BATTERY

Subject Name: Subject Code:

Date Tested:_____ Time of Testing: _____/_____
MM / DD / YY hh / mm

QUESTIONNAIRES (Take-Home)

Date Returned: _____
MM / DD / YY

(X)	Completed
Revised NEO Personality Inventory (NEO PI-R)	_____
Beck Depression Inventory (BDI)	_____
State Trait Anxiety Inventory (STAI)	_____
Headache Questionnaire	_____

Notes: _____

NEUROPSYCHOLOGICAL BATTERY

French _____ English _____ Check When Done (X)

Handedness Questionnaire _____

WMS-R: Stories (Imm Presentation) / TIME _____ _____
90 min Delay Recall

Rey Figure (Copy) / TIME _____ _____
40 min Delayed Recall

Rey Figure (Immediate Recall) _____

WASI: Vocabulary _____
Block Design _____
Similarities _____
Matrices _____

Rey Figure (Delayed Recall) _____

WMS-III: Memory for Faces I / TIME _____ _____
25-35 min Delayed Recall
Letter-Number Sequencing _____

Word Fluency (FAS) & Animal Fluency _____

WMS-III: Memory for Faces II (Delayed Recall) _____

WMS-R: Stories (Delayed Recall) _____

CVLT-II (Immediate Presentation) / TIME _____ _____
20 min Delayed Recall

WMS-III: Digit Span Forward _____
Digit Span Backward _____

Stroop Test _____

Tapping _____

CVLT-II (20 min Delayed Recall) _____

Grooved Pegboard _____

Pinch Strength _____

CVLT-II (10 min Forced-Choice Recognition) _____

CANTAB: Motor Screening (2 min) _____
Spatial Span (7-10 min) _____
Match to sample Visual Search (10 min) _____
Spatial Working Memory (7-10 min) _____
Paired Associates Learning (8-10 min) _____
Intra Dimensional / Extra Dimensional Attention Shift (10 min) _____
Stockings of Cambridge (8-10 min) _____
Rapid Visual Information Processing (10 min) _____

APPENDIX H

Handedness Questionnaire

– English and French Versions –

HANDEDNESS QUESTIONNAIRE

Handedness _____ (Strongly or moderately) _____

Handedness history:

Conversion? (by authority or accident) _____

Tasks not performed by the dominant hand (ask particularly about sports, e.g., tennis, golf, baseball) _____

_____

Practical (has either hand been trained to do a specific task?)

Family handedness (if the patient does not know, contact the family)

Handedness			Handedness		
Father		_____	Mother		_____
Brother	1.	_____	Sister	1.	_____
	2.	_____		2.	_____
	3.	_____		3.	_____
	4.	_____		4.	_____
Paternal Side			Maternal Side		
Grandfather		_____	Grandfather		_____
Grandmother		_____	Grandmother		_____
Uncles	1.	_____	Uncles	1.	_____
	2.	_____		2.	_____
Aunts	1.	_____	Aunts	1.	_____
	2.	_____		2.	_____

MANUAL LATERALIZATION

		Column 1	Column 2
R_a –	Right hand always	1	5
R_m –	Right hand most of the time	2	4
E –	Both hands equally often	3	3
L_a –	Left hand most of the time	4	2
L_m –	Left hand always	5	1

Which hand do you normally use to:	**Answer**	(1) **1-5**	(2) **1-5**
1. Hold scissors when cutting		___	___
2. Throw a ball		___	___
3. Hold a slice of bread when buttering		___	___
4. Hold a watch when setting the time		___	___
5. Hold a glass when drinking		___	___
6. Hold a needle when threading		___	___
7. Hold a dish when wiping		___	___
8. Put a key into a lock		___	___
9. Hold a pencil when writing		___	___
10. Hold a comb when combing hair		___	___
11. Hold a bottle when unscrewing the top		___	___
12. Hold a potato when peeling		___	___
13. Hold a toothbrush when brushing teeth		___	___
14. Dial a telephone number		___	___
15. Hold a pitcher when pouring out of it		___	___
16. Turn on a single water tap		___	___
17. Hold a loaf of bread when you cutting with a knife		___	___
18. Hold a nail when hammering		___	___
	Sous totaux	___	___
	Score Total		___/90

QUESTIONNAIRE DE LA LATERALIZATION MANUELLE

Latéralisation manuelle _____ Forte ou modérée ___

Renseignements:

Conversion – (par correction ou par accident) _____

Tâches non effectuées par la main dominante (demander plus particulièrement pour les sports, par exemple tennis, golf, baseball) _____

_____

Pratique (est-ce qu'une main a été entraînée à faire une tâche particulière ?)

_____

_____

Latéralisation manuelle familiale (si le patient ne le sait pas, contacter la famille)

Latéralisation manuelle

Père _____

Frère 1._____
2. _____
3. _____
4. _____

Latéralisation manuelle

Mère _____

Sœur 1. _____
2. _____
3. _____
4. _____

Côté Paternel

Grand-père _____
Grand-mère _____
Oncles 1._____
2. _____
Tantes 1._____
2. _____

Côté Maternel

Grand-père _____
Grand-mère _____
Oncles 1. _____
2. _____
Tantes 1. _____
2. _____

LATÉRALISATION MANUELLE

	Colonne 1	Colonne 2
R_a – main droite toujours	1	5
R_m – main droite la plupart du temps	2	4
E – l'un ou l'autre main	3	3
L_a – main gauche la plupart du temps	4	2
L_m – main gauche toujours	5	1

Quelle main utilisez vous habituellement pour :	(1)	(2)
Réponse	1-5	1-5
1. Tenir des ciseaux quand vous coupez quelque chose	___	___
2. Lancer une balle	___	___
3. Tenir une tranche de pain quand vous la beurrez	___	___
4. Tenir une montre quand vous ajuster l'heure	___	___
5. Tenir un verre quand vous buvez	___	___
6. Tenir une aiguille quand vous enfilez du fil	___	___
7. Tenir l'assiette quand vous essuyez la vaisselle	___	___
8. mettre une clef dans une serrure	___	___
9. Tenir votre crayon quand vous écrivez	___	___
10. Tenir votre peigne quand vous vous coiffez	___	___
11. Tenir une bouteille de liqueur douce quand vous la décapsulez	___	___
12. Tenir une pomme de terre quand vous la pelez	___	___
13. Tenir votre brosse à dents	___	___
14. Signaler un numéro de téléphone	___	___
15. Tenir un pichet (pot d'eau) quand vous versez dans un verre	___	___
16. Ouvrir un robinet quand il n'y en a qu'un	___	___
17. Tenir une miche de pain quand vous la coupez avec un couteau	___	___
18. Tenir un clou vous le frappez avec un marteau	___	___
Sous totaux	___	___
Score Total		___/90

APPENDIX I

California Verbal Learning Test – 2nd Edition

– French Version –

Liste A Rappel libre immédiat

Essai 1

Je vais vous lire une liste de mots. Ecoutez attentivement car par la suite, je vais vous demander de me répéter le plus grand nombre de mots que possible. Vous pouvez dire les mots dans n'importe quel ordre.

Essai 2

Je vais relire la même liste à nouveau. Comme auparavant, dites moi le plus grand nombre de mots que possible Vous pouvez dire les mots dans n'importe quel ordre. Dites-les moi tous.

Essai 3 & 4

Je vais lire la même liste de nouveau. Comme auparavant, dites moi le plus grand nombre de mots dans n'importe quel ordre. Dites-les moi tous.

Essai 5

Je vais lire la même liste une dernière fois. Comme auparavant, dites moi le plus grand nombre de mots ds. n'importe quel ordre Dites-les moi tous.

Prêt(e)?

Noter toutes les réponses dans l'ordre évoqué. Inviter une seule fois (Autre chose?) à la fin de chaque rappel libre ainsi que à la fin de chaque rappel avec signal.

Approximativement 1 mot/sec.
Dites: Allez-y!

Liste A		Essai 1	Type Rép	Essai 2	Type Rép	Essai 3	Type Rép	Essai 4	Type Rép	Essai 5	Type Rép
Camion	1										
Épinard	2										
Giraffe	3										
Bibliothèque	4										
Oignon	5										
Motocyclette	6										
Cabinet	7										
Zèbre	8										
Métro	9										
Lampe	10										
Céleri	11										
Vache	12										
Bureau	13										
Bateau	14										
Écureuil	15										
Chou	16										
	17										
	18										
	19										
	20										
	Total Correct	C		C		C		C		C	
	Total Répétitions	R		R		R		R		R	
	Total Intrusions	I		I		I		I		I	

Liste B Rappel Libre Immédiat

Maintenant je vais vous lire une 2ème liste de mots. A la fin, redites moi le plus grand nombre de mots de cette liste, dans n'importe quel ordre. Ne me dites pas de mots sur la 1ère liste, juste de la 2ème.

Liste A Rappel Libre Court-Délai

Maintenant dites moi tous les mots de la 1ère liste, celle que j'ai lu plusieurs fois. Ne me dites pas des mots de la 2ème liste, juste de la 1ère. Allez-y!

Liste A Rappel Avec Indices Court-Délai

Dites moi tous les mots de la 1ère liste qui sont des meubles.
Dites moi tous les mots de la 1ère liste qui sont des légumes.
Dites moi tous les mots de la 1ère liste qui sont des moyens de transport.
Dites moi tous les mots de la 1ère liste qui sont des animaux.

Noter toutes les réponses dans l'ordre évoqué. Inviter une seule fois (Autre chose?) à la fin de chaque rappel libre ainsi que à la fin de chaque rappel avec indices.

Approximativement 1 mot/sec.
Dites: Allez-y!

Liste B		Liste B	Type Rép	Liste A	Type Rép
	1				
Violon	2				
Concombre	3				
Éléphant	4				
Garde-robe	5				
Navet	6				
Guitare	7				
Sous-sol	8				
Mouton	9				
Clarinette	10				
Garage	11				
Maïs	12				
Lapin	13				
Patio	14				
Saxophone	15				
Tigre	16				
Radis	17				
	18				
	19				
	20				
	Total Correct	C		C	
	Total Répétitions	R		R	
	Total Intrusions	I		I	

Meubles	Type Rép	Légumes	Type Rép
1			
2			
3			
4			
5			
6			
7			
8			

Moyens de Transport	Type Rép	Animaux	Type Rép
1			
2			
3			
4			
5			
6			
7			
8			
		Total Correct C	
		Total Répétitions R	
		Total Intrusions I	

Rappel différé: environ 20-minutes entre le rappel avec indices et le début du rappel libre. Ne mentionnez pas au sujet qu'il va y'en avoir d'autres essaies.

Liste A Rappel Libre Long-Délai

J'ai vous ai lu deux listes de mots. J'ai lu la 1ère liste plusieurs fois et la 2ème liste juste une fois. Dites moi tous les mots de la 1ère liste. Ne me dites pas de mots de la 2ème liste. Allez-y!

Liste A Rappel Avec Indices Long-Délai

Dites moi tous les mots de la 1ère liste qui sont des meubles.
Dites moi tous les mots de la 1ère liste qui sont des légumes.
Dites moi tous les mots de la 1ère liste qui sont des moyens de transport.
Dites moi tous les mots de la 1ère liste qui sont des animaux.

Essai 1	Type Rép	Meubles	Type Rép	Legumes	Type Rép	Moyens de Transport	Type Rép	Animaux	Type Rép
1									
2									
3									
4									
5									
6									
7									
8									
9				C		R		I	
10									
11									
12									
13									
14									
15									
16									
17									
18									
19									
20									
Correct									
Repetition									
Intrusions									

Liste A Reconnaissance Différée Oui/Non

Maintenant je vais vous lire une liste de mots. Après chaque mot, dites Oui si le mot appartient à la 1ère liste ou dites Non si le mot n'etait pas sur la 1ère liste.

	Rép			Rép			Rép			Rép		
Portofeuille	Y	N	UN	Violon	Y	N	BN	Chien	Y	N	PR	Navet	Y	N	BS
Bateau	Y	N	T	Vache	Y	N	T	Bibliothèque	Y	N	T	Cabinet	Y	N	T
Saxophone	Y	N	BN	Fourchette	Y	N	UN	Allumette	Y	N	UN	Oignon	Y	N	T
Concombre	Y	N	BS	Autobus	Y	N	PR	Epinard	Y	N	T	Lion	Y	N	PR
Giraffe	Y	N	T	Céleri	Y	N	T	Clarinette	Y	N	BN	Caméra	Y	N	UN
Carotte	Y	N	PR	Lampe	Y	N	T	Camion	Y	N	T	Guitare	Y	N	BN
Patio	Y	N	BN	Radis	Y	N	BS	Lapin	Y	N	BS	Métro	Y	N	T
Chou	Y	N	T	Table	Y	N	PR	Chaise	Y	N	PR	Tigre	Y	N	BS
Bureau	Y	N	T	Rose	Y	N	UN	Maïs	Y	N	BS	Café	Y	N	UN
Bracelet	Y	N	UN	Motocyclette	Y	N	T	Coquillage	Y	N	UN	Zèbre	Y	N	T
Voiture	Y	N	PR	Mouton	Y	N	BS	Garage	Y	N	BN	Laitue	Y	N	PR
Éléphant	Y	N	BS	Sous-Sol	Y	N	BN	Ecureuil	Y	N	T	Garde-Robe	Y	N	BN

Total Correct = _____ Total Fause Positives = _____

Laisser environ **10-minutes** entre la tâche de reconnaissance OUI/NON et le début de la reconnaissance forcée.

Liste A Reconnaissance forcée (optionnelle)

Tantôt, Je vous ai lu de listes des mots, vous vous en souvenez? Maintenant je vais vous lire deux mots à la fois. Après chaque paire de mots, vous devez me dire lequel des deux mots était sur la 1ère liste, celle que j'ai lu plusieurs foix. Il peut être difficile de s'en souvenir, mais faite de votre mieux. Prêt(e)?
Est ce que c'était bateau ou drapeau sur la 1ère liste?
Est ce que c'était _____ ou _____ sur la 1ère liste?

NOTES

			Score (1 / 0)	Type Dist
Bateau	ou	Drapeau		C
Gateau	ou	**Bureau**		C
Majorité	ou	**Vache**		A
Céleri	ou	Aspirine		C
Bibliothèque	ou	Silence		A
Mélangeur	ou	**Camion**		C
Oignon	ou	Logique		A
Baseball	ou	**Zèbre**		C
Instruction	ou	**Cabinet**		A
Écureuil	ou	Direction		A
Couverture	ou	**Chou**		C
Métro	ou	Technique		A
Hauteur	ou	**Epinard**		A
Giraffe	ou	Serviette		C
Sujet	ou	**Motocyclette**		A
Lampe	ou	Gicleur		C
Total Correct				

Total Correct: (_____ / 16) x 100 = _____ %

APPENDIX J

Wechsler Memory Scale: Logical Memory Passages

– French Version –

WMS (Form I)

Jeanne Duval / de Montréal / Est / employée / comme femme de ménage / dans un édifice à bureau / est allée au poste de police / où elle a raconté / que la veille / un homme aux cheveux gris / lui avait volé / soixante-quinze dollars / sur la rue Ste Catherine. / Elle avait quatre / petits enfants / le loyer / n'était pas payé / et ça faisait déjà deux jours / qu'ils n'avaient pas mangé. / Les policiers / touchés par ce triste récit / ont donné de l'argent / à la pauvre femme.

Score A: /23

Le navire / canadien / Reine de France / a frappé un iceberg / lundi soir / près de la Nouvelle-Ecosse. / Malgré une tempête de neige / aveuglante / et la nuit obscure / on a sauvé / les 300 / passagers, dont 18 / femmes / même si les chaloupes de sauvetage / ballottaient / comme des bouchons / sur la mer déchaînée. / Le lendemain / un bateau à vapeur / britannique / les a guidés jusqu'au port. /

Score B: /23

Total Score: (A + B) / 2 = /23

APPENDIX K

Verbal Fluency Test

VERBAL FLUENCY TEST – Record Form

Verbal Fluency Time Limit: 60 seconds per item

Time	Semantic		Phonemic		
	Animals	Food or Drink	S	F	A
1- 15"					
16-30"					
31-45"					
46-60"					
Total Words					

APPENDIX L

Stroop Test

– English and French Scoring Forms –

STROOP TEST – Scoring Form

Colour (# in 45")

red	blue	green	red	blue	red	green	red	green	blue
red	blue	green	blue	red	green	red	blue	green	red
red	green	blue	red	green	red	blue	green	red	green
green	red	blue	green	blue	green	red	blue	blue	red
red	green	blue	green	red	green	blue	red	blue	green
blue	green	blue	red	blue	red	green	blue	red	green
green	red	blue	red	green	blue	red	red	green	blue
blue	red	blue	green	red	blue	green	red	blue	red
green	blue	green	blue	red	green	red	blue	green	red
blue	red	blue	green	red	blue	green	red	blue	red

Score: _____ (No Correct Responses + No Corrected Errors)

Corrected Errors: _____ Non-corrected Errors: _____

Word (# in 45")

red	blue	red	green	blue	red	green	blue	red	blue
red	green	blue	red	green	red	blue	green	blue	green
red	blue	red	green	blue	red	green	blue	red	blue
blue	green	red	red	blue	green	red	blue	red	green
green	red	blue	green	red	blue	red	blue	green	blue
green	blue	red	blue	green	red	green	blue	green	red
red	blue	blue	red	green	blue	green	blue	red	green
green	red	green	blue	red	green	red	blue	green	red
red	green	blue	red	green	red	blue	green	blue	red
blue	green	red	green	red	blue	red	green	blue	red

Score: _____ (No Correct Responses + No Corrected Errors)

Corrected Errors: _____ Non-corrected Errors: _____

Colour-Word (# in 45")

blue	green	blue	blue	red	green	red	blue	green	red
green	red	blue	green	blue	red	green	red	blue	green
blue	red	green	blue	red	green	red	blue	green	red
blue	green	red	blue	red	blue	green	red	green	blue
blue	red	green	blue	green	red	green	blue	green	blue
red	blue	green	blue	red	green	red	green	blue	red
red	blue	red	green	red	green	blue	green	red	green
red	blue	red	blue	green	red	blue	green	red	blue
blue	green	blue	red	blue	red	blue	green	red	green
red	blue	green	red	blue	green	blue	green	red	green

Score: _____ (No Correct Responses + No Corrected Errors)

Corrected Errors: _____ Non-corrected Errors: _____

SUMMARY RESULTS

Colour

Score: _____

Corrected Errors: _____

Non-corrected Errors: _____

Word

Score: _____

Corrected Errors: _____

Non-corrected Errors: _____

Colour-Word

Score: _____

Corrected Errors: _____

Non-corrected Errors: _____

TEST DE STROOP – Forme des Résultats

Nommer la couleur (# dans 45")

rouge	bleu	vert	rouge	bleu	rouge	vert	rouge	vert	bleu
rouge	bleu	vert	bleu	rouge	vert	rouge	bleu	vert	rouge
rouge	vert	bleu	rouge	vert	rouge	bleu	vert	rouge	vert
vert	rouge	bleu	vert	bleu	vert	rouge	bleu	bleu	rouge
rouge	vert	bleu	vert	rouge	vert	bleu	rouge	bleu	vert
bleu	vert	bleu	rouge	bleu	rouge	vert	bleu	rouge	vert
vert	rouge	bleu	rouge	vert	bleu	rouge	rouge	vert	bleu
bleu	rouge	bleu	vert	rouge	bleu	vert	rouge	bleu	rouge
vert	bleu	vert	bleu	rouge	vert	rouge	bleu	vert	rouge
bleu	rouge	bleu	vert	rouge	bleu	vert	rouge	bleu	rouge

Résultat: _____ (No Réponses Correctes + No Erreurs corrigées)

Erreurs corrigées: _____ Erreurs non corrigées: _____

Lire le mot (# dans 45")

rouge	bleu	rouge	vert	bleu	rouge	vert	bleu	rouge	bleu
rouge	vert	bleu	rouge	vert	rouge	bleu	vert	bleu	vert
rouge	bleu	rouge	vert	bleu	rouge	vert	bleu	rouge	bleu
bleu	vert	rouge	rouge	bleu	vert	rouge	bleu	rouge	vert
vert	rouge	bleu	vert	rouge	bleu	rouge	bleu	vert	bleu
vert	bleu	rouge	bleu	vert	rouge	vert	bleu	vert	rouge
rouge	bleu	bleu	rouge	vert	bleu	vert	bleu	rouge	vert
vert	rouge	vert	bleu	rouge	vert	rouge	bleu	vert	rouge
rouge	vert	bleu	rouge	vert	rouge	bleu	vert	bleu	rouge
bleu	vert	rouge	vert	rouge	bleu	rouge	vert	bleu	rouge

Résultat: _____ (No Réponses Correctes + No Erreurs corrigées)

Erreurs corrigées: _____ Erreurs non corrigées: _____

Couleur de l'encre (# dans 45")

bleu	vert	bleu	bleu	rouge	vert	rouge	bleu	vert	rouge
vert	rouge	bleu	vert	bleu	rouge	vert	rouge	bleu	vert
bleu	rouge	vert	bleu	rouge	vert	rouge	bleu	vert	rouge
bleu	vert	rouge	bleu	rouge	bleu	vert	rouge	vert	bleu
bleu	rouge	vert	bleu	vert	rouge	vert	bleu	vert	bleu
rouge	bleu	vert	bleu	rouge	vert	rouge	vert	bleu	rouge
rouge	bleu	rouge	vert	rouge	vert	bleu	vert	rouge	vert
rouge	bleu	rouge	bleu	vert	rouge	bleu	vert	rouge	bleu
bleu	vert	bleu	rouge	bleu	rouge	bleu	vert	rouge	vert
rouge	bleu	vert	rouge	bleu	vert	bleu	vert	rouge	vert

Résultat: _____ (No Réponses Correctes + No Erreurs corrigées)

Erreurs corrigées: _____ Erreurs non corrigées: _____

SOMMAIRE DES RESULTATS

Couleur

Résultat: _____
Erreurs corrigées: _____
Erreurs non corrigées: _____

Mot

Résultat: _____
Erreurs corrigées: _____
Erreurs non corrigées: _____

Couleur-Mot

Résultat: _____
Erreurs corrigées: _____
Erreurs non corrigées: _____

APPENDIX M

Cambridge Neuropsychological Test Automated Battery

(CANTAB)

The Intradimensional/Extradimensional (ID/ED) Set-Shifting

The Stockings of Cambridge (Tower of London) subtest

APPENDIX N

Tapping Test

TAPPING TEST

SEQUENTIAL TAPPING

Hand	Trial[1]	Counter Reading	No Errors	No Correct
Left □	1			
Right □	5			
Left □	2			
Right □	4			
Both	3			
	6			

[1]Trials 1 to 6: administration time for each trial is 30 seconds.

SINGLE TAPPING

Hand	Trial[2]	Counter Reading
Left □	7	
Right □		
Left □	8	
Right □		

[2]Administration time for each trial is 15 seconds.

SUMMARY RESULTS

	Mean Correct Score		Total No Errors
Left Hand	_____	Left Hand	_____
Right Hand	_____	Right Hand	_____

APPENDIX O

Grooved Pegboard Test

GROOVED PEGBOARD TEST

Trial 1
Hand: Left □ / Right □

1. _____ sec
2. _____ sec
3. _____ sec
4. _____ sec
5. _____ sec

No Pegs Dropped _____

Trial 2
Hand: Left □ / Right □

1. _____ sec
2. _____ sec
3. _____ sec
4. _____ sec
5. _____ sec

No Pegs Dropped _____

Trial 3
Hand: Left □ / Right □

1. _____ sec
2. _____ sec
3. _____ sec
4. _____ sec
5. _____ sec

No Pegs Dropped _____

Trial 4
Hand: Left □ / Right □

1. _____ sec
2. _____ sec
3. _____ sec
4. _____ sec
5. _____ sec

No Pegs Dropped _____

RESULTS

Mean Score (sec)		Total No Pegs Dropped	
Left Hand	_____	Left Hand	_____
Right Hand	_____	Right Hand	_____

Total No Pegs Dropped (All 4 Trials)

APPENDIX P

Pinch Strength Test

PINCH STRENGTH TEST

Trial 1
Hand: Left □ / Right □

_____

Trial 2
Hand: Left □ / Right □

_____

Trial 3
Hand: Left □ / Right □

_____

Trial 4
Hand: Left □ / Right □

_____

Trial 5
Hand: Left □ / Right □

_____

Trial 6
Hand: Left □ / Right □

_____

RESULTS			
Mean Score (sec)			
Left Hand	_____	Right Hand	_____

APPENDIX Q

Emotion & Personality Measures: Means and Standard Deviations and Non-Significant ANOVA Results

Table Q-1

Emotional Status and Personality Traits: Non-Significant ANOVA Results

Variable	df	SS	MS	F	p	Power
ASTAI - State Anxiety						
Group	4	28.96	7.24	0.05	0.995	0.06
Hemisphere	2	1.62	0.81	0.01	0.994	0.05
Type	2	2.41	1.21	0.01	0.991	0.05
ASTAI - Trait Anxiety						
Group	4	459.62	114.91	1.12	0.361	0.31
Hemisphere	2	313.38	156.69	1.53	0.230	0.30
Type	2	267.51	133.75	1.31	0.283	0.26
Beck Depression Index						
Group	4	213.83	53.46	1.10	0.374	0.31
Hemisphere	2	174.37	87.19	1.79	0.182	0.35
Type	2	192.97	96.48	1.98	0.154	0.38
NEOPI - Extroversion						
Group	4	3460.76	865.19	2.24	0.086	0.59
Hemisphere	2	1215.31	607.65	1.57	0.223	0.31
Type	2	638.90	319.45	0.83	0.447	0.18
NEOPI - Agreeableness						
Group	4	1544.96	386.24	1.02	0.409	0.29
Hemisphere	2	806.81	403.40	1.07	0.354	0.22
Type	2	642.79	321.40	0.85	0.435	0.18
NEOPI - Conscientiousness						
Group	4	1232.77	308.19	0.69	0.601	0.20
Hemisphere	2	397.05	198.53	0.45	0.643	0.12
Type	2	4.26	2.13	0.00	0.995	0.05

Table Q-2

Means and Standard Deviations for Emotion and Personality Measures

Variable	N	Mean	SD
STAI - State Anxiety			
NC	10	35.60	15.45
MO_{Right}	10	34.05	10.06
MO_{Left}	7	35.92	12.18
MA_{Right}	7	36.20	10.32
MA_{Left}	5	34.37	6.81
STAI - Trait Anxiety			
NC	10	37.60	14.32
MO_{Right}	10	36.80	7.39
MO_{Left}	7	41.47	6.54
MA_{Right}	7	40.80	7.69
MA_{Left}	5	47.49	11.44
Beck Depression Inventory			
NC	10	4.30	10.15
MO_{Right}	10	6.95	3.52
MO_{Left}	7	9.14	5.24
MA_{Right}	7	10.29	7.78
MA_{Left}	5	10.20	4.71
NEOPI-Neuroticism			
NC	10	73.30	29.74
MO_{Right}	10	80.70	19.89
MO_{Left}	7	86.37	18.9
MA_{Right}	7	99.20	25.91
MA_{Left}	5	110.12	18.49
NEOPI-Extroversion			
NC	10	112.50	26.55
MO_{Right}	10	95.67	20.15
MO_{Left}	7	121.80	14.54
MA_{Right}	7	104.60	11.97
MA_{Left}	5	99.22	16.07
NEOPI-Openness to Experience			
NC	10	128.00	11.53
MO_{Right}	10	102.67	18.72
MO_{Left}	7	118.37	12.61
MA_{Right}	7	102.60	11.51
MA_{Left}	5	114.22	21.61

Table Q-2

Means and Standard Deviations for Emotion and Personality Measures (continued)

Variable	N	Mean	SD
NEOPI-Agreeableness			
NC	10	114.40	22.52
MO_{Right}	10	104.92	19.27
MO_{Left}	7	116.57	25.57
MA_{Right}	7	115.40	8.75
MA_{Left}	5	125.48	11.59
NEOPI-Conscientiousness			
NC	10	120.30	20.43
MO_{Right}	10	118.25	24.59
MO_{Left}	7	122.77	19.46
MA_{Right}	7	129.60	17.17
MA_{Left}	5	109.86	21.46

APPENDIX R

Means and Standard Deviations for Cognitive & Motor Measures

Table R-1

Means and Standard Deviations for Overall Cognitive Measures

Variable[1]	N	Mean	SD
Full Scale IQ			
NC	10	119.40	12.47
MO_{Right}	10	110.30	10.68
MO_{Left}	7	108.86	9.53
MA_{Right}	7	94.14	6.44
MA_{Left}	5	105.00	12.02
Verbal IQ			
NC	10	121.20	11.04
MO_{Right}	10	108.50	16.48
MO_{Left}	7	108.29	14.20
MA_{Right}	7	93.29	10.64
MA_{Left}	5	94.60	15.69
Performance IQ			
NC	10	113.60	15.65
MO_{Right}	10	109.60	13.56
MO_{Left}	7	109.71	11.80
MA_{Right}	7	96.43	8.87
MA_{Left}	5	115.00	12.06
Vocabulary			
NC	10	64.30	6.09
MO_{Right}	10	55.80	13.46
MO_{Left}	7	55.14	10.56
MA_{Right}	7	46.00	10.44
MA_{Left}	5	46.80	15.24
Block Design			
NC	10	59.30	10.72
MO_{Right}	10	55.10	5.80
MO_{Left}	7	54.43	9.69
MA_{Right}	7	48.43	12.92
MA_{Left}	5	57.20	6.98
Similarities			
NC	10	60.80	7.15
MO_{Right}	10	55.00	9.14
MO_{Left}	7	54.86	7.65
MA_{Right}	7	44.71	7.52
MA_{Left}	5	46.00	8.94

Table R-1

Means and Standard Deviations for Overall Cognitive Measures (continued)

Variable	N	Mean	SD
Matrix Reasoning			
NC	10	56.00	8.79
MO_{Right}	10	57.40	9.62
MO_{Left}	7	57.14	5.18
MA_{Right}	7	47.57	9.69
MA_{Left}	5	60.60	5.46

Note. [1]NC = Normal control subjects; MO_{Right} = patients without aura with right-sided migraine; MO_{Left} = patients without aura with left-sided migraine; MA_{Right} = patients with aura with right-sided migraine; MA_{Left} = patients with aura with left-sided migraine.

Table R-2

Means and Standard Deviations for Attention & Concentration Measures

Variable	N	Mean	SD
Digit Span Forward - Raw			
NC	10	11.50	2.07
MO_{Right}	10	10.30	1.57
MO_{Left}	7	9.43	1.90
MA_{Right}	7	9.86	1.21
MA_{Left}	5	10.80	1.48
Digit Span Forward - Length			
NC	10	7.30	0.95
MO_{Right}	10	6.30	0.67
MO_{Left}	7	6.14	0.90
MA_{Right}	7	6.29	0.76
MA_{Left}	5	7.00	1.22
Digit Span Forward Total			
NC	10	19.8	4.02
MO_{Right}	10	17.00	1.89
MO_{Left}	7	17.00	3.37
MA_{Right}	7	17.00	3.61
MA_{Left}	5	18.40	4.04
Stroop - Color			
NC	10	81.60	15.14
MO_{Right}	10	75.30	12.38
MO_{Left}	7	74.71	11.31
MA_{Right}	7	77.14	10.38
MA_{Left}	5	82.00	11.83
Stroop - Word			
NC	10	114.40	17.12
MO_{Right}	10	105.30	15.88
MO_{Left}	7	101.57	13.61
MA_{Right}	7	97.00	13.1
MA_{Left}	5	111.80	13.01
Spatial Span Length			
NC	10	6.14	1.37
MO_{Right}	10	6.00	0.67
MO_{Left}	7	6.17	1.34
MA_{Right}	7	6.50	0.50
MA_{Left}	5	7.80	0.84

Table R-2

Means and Standard Deviations for Attention & Concentration Measures (continued)

Variable	N	Mean	SD
Rapid Visual Processing			
NC	10	0.92	0.06
MO_{Right}	10	0.92	0.02
MO_{Left}	7	0.93	0.05
MA_{Right}	7	0.89	0.05
MA_{Left}	5	0.92	0.03

Table R-3

Means and Standard Deviations for Verbal Memory Measures

Variable	N	Mean	SD
WMS-R Stories[1]			
A-IR			
NC	10	12.15	3.05
MO_{Right}	10	10.40	3.06
MO_{Left}	7	12.64	5.54
MA_{Right}	7	11.79	2.98
MA_{Left}	5	11.00	3.48
B-IR			
NC	10	9.75	2.54
MO_{Right}	10	8.65	3.14
MO_{Left}	7	7.50	3.19
MA_{Right}	7	8.50	1.96
MA_{Left}	5	7.50	2.32
Mean IR			
NC	10	10.95	2.18
MO_{Right}	10	9.53	2.63
MO_{Left}	7	10.07	3.93
MA_{Right}	7	10.14	2.34
MA_{Left}	5	9.25	2.84
A-DR			
NC	10	10.15	3.14
MO_{Right}	10	8.35	3.51
MO_{Left}	7	9.57	3.97
MA_{Right}	7	9.43	2.62
MA_{Left}	5	9.60	2.01
B-DR			
NC	10	8.10	2.79
MO_{Right}	10	7.35	2.91
MO_{Left}	7	6.79	3.63
MA_{Right}	7	7.64	1.70
MA_{Left}	5	7.20	2.89
Mean DR			
NC	10	9.13	2.45
MO_{Right}	10	7.85	2.68
MO_{Left}	7	8.18	3.13
MA_{Right}	7	8.54	1.85
MA_{Left}	5	8.40	2.08

Table R-3

Means and Standard Deviations for Verbal Memory Measures (continued)

Variable		N	Mean	SD
CVLT-II[2]				
T1	NC	10	7.30	2.26
	MO_{Right}	10	6.40	1.90
	MO_{Left}	7	6.71	2.50
	MA_{Right}	7	5.71	0.95
	MA_{Left}	5	6.80	0.84
T2	NC	10	10.20	3.05
	MO_{Right}	10	10.70	2.71
	MO_{Left}	7	11.00	3.42
	MA_{Right}	7	9.00	2.24
	MA_{Left}	5	9.80	3.03
T3	NC	10	11.70	2.06
	MO_{Right}	10	11.40	2.46
	MO_{Left}	7	11.29	2.87
	MA_{Right}	7	11.14	3.02
	MA_{Left}	5	12.00	2.55
T4	NC	10	13.80	2.74
	MO_{Right}	10	11.90	3.14
	MO_{Left}	7	13.43	2.99
	MA_{Right}	7	12.43	2.64
	MA_{Left}	5	12.60	2.61
T5	NC	10	14.40	1.51
	MO_{Right}	10	13.00	2.58
	MO_{Left}	7	13.00	2.16
	MA_{Right}	7	11.71	2.36
	MA_{Left}	5	13.80	1.30
T1 to T5	NC	10	58.10	9.76
	MO_{Right}	10	52.40	12.55
	MO_{Left}	7	55.43	12.46
	MA_{Right}	7	50.00	10.13
	MA_{Left}	5	55.00	8.63
TB	NC	10	6.10	2.64
	MO_{Right}	10	5.00	1.56
	MO_{Left}	7	7.57	1.99
	MA_{Right}	7	5.71	1.25
	MA_{Left}	5	5.40	1.34

Table R-3

Means and Standard Deviations for Verbal Memory Measures (continued)

Variable		N	Mean	SD
SDFREE	NC	10	13.40	2.59
	MO_{Right}	10	11.20	3.52
	MO_{Left}	7	10.29	2.63
	MA_{Right}	7	10.00	2.89
	MA_{Left}	5	11.60	1.82
SDCUED	NC	10	13.70	2.41
	MO_{Right}	10	12.60	3.31
	MO_{Left}	7	11.86	2.41
	MA_{Right}	7	10.86	1.86
	MA_{Left}	5	12.60	2.70
LDFREE	NC	10	13.90	2.28
	MO_{Right}	10	11.00	4.11
	MO_{Left}	7	11.43	2.99
	MA_{Right}	7	10.29	3.64
	MA_{Left}	5	12.80	2.17
LDCUED	NC	10	14.00	2.31
	MO_{Right}	10	11.80	3.39
	MO_{Left}	7	11.86	2.85
	MA_{Right}	7	11.29	2.43
	MA_{Left}	5	11.80	2.59

Note. [1]A-IR = immediate recall story A; B-IR = immediate recall story B; Mean IR = A & B mean immediate recall; A-DR = delayed recall story A; B-DR = delayed recall story B; Mean DR = A & B mean delayed recall.

[2]T1 = Trial 1 recall; T2 = Trial 2 recall; T3 = Trial 3 recall; T4 = Trial 4 recall; T5 = Trial 5 recall; T1 to T5 = Recall for trials 1 to 5; TB = Trial B recall; SDFREE = short delay free recall; SDCUED = short delay cued recall; LDCUED = long delay free recall; LDFREE = long delay cued recall.

Table R-4

Means and Standard Deviations for Visuo-Spatial Memory Measures

Variable[1]	N	Mean	SD
Rey Figure IR			
NC	10	17.00	7.21
MO_{Right}	10	10.80	5.40
MO_{Left}	7	13.14	6.34
MA_{Right}	7	11.71	3.26
MA_{Left}	5	14.60	3.36
Rey Figure IR (sec)			
NC	10	149.40	30.46
MO_{Right}	10	136.20	43.64
MO_{Left}	7	138.00	38.00
MA_{Right}	7	98.29	21.94
MA_{Left}	5	156.60	19.92
Rey Figure DR			
NC	10	15.80	5.00
MO_{Right}	10	10.40	5.02
MO_{Left}	7	13.00	6.84
MA_{Right}	7	10.71	3.47
MA_{Left}	5	13.80	2.25
Rey Figure DR (sec)			
NC	10	106.80	31.96
MO_{Right}	10	91.90	26.23
MO_{Left}	7	107.57	24.74
MA_{Right}	7	88.57	33.44
MA_{Left}	5	101.20	30.78
WMS-III Faces IR			
NC	10	37.40	4.55
MO_{Right}	10	38.60	3.84
MO_{Left}	7	39.86	3.29
MA_{Right}	7	37.14	2.73
MA_{Left}	5	39.20	5.02

Table R-4

Means and Standard Deviations for Visuo-Spatial Memory Measures (continued)

Variable	N	Mean	SD
WMS-III Faces DR			
NC	10	37.40	3.78
MO_{Right}	10	37.10	5.20
MO_{Left}	7	37.57	5.03
MA_{Right}	7	39.43	4.31
MA_{Left}	5	39.40	2.70

Note. [1]Rey Figure IR = Immediate Recall; Rey Figure IR (sec) = Immediate Recall Time; Rey Figure DR = Delayed Recall; Rey Figure DR (sec) = Delayed Recall Time; WMS-III Faces IR = Faces Immediate Recall; WMS-III Faces DR = Faces Delayed Recall.

Table R-5

Means and Standard Deviations for Working Memory Measures

Variable[1]	N	Mean	SD
WMS-III Letter/Number			
NC	10	11.60	2.88
MO_{Right}	10	11.50	2.12
MO_{Left}	7	12.29	1.50
MA_{Right}	7	10.43	3.26
MA_{Left}	5	12.60	2.30
Digit Span Backward - Raw			
NC	10	8.30	2.21
MO_{Right}	10	6.70	1.42
MO_{Left}	7	7.57	2.30
MA_{Right}	7	7.14	2.73
MA_{Left}	5	7.60	3.29
Digit Span Backward - Length			
NC	10	5.70	1.34
MO_{Right}	10	5.10	1.29
MO_{Left}	7	5.29	1.60
MA_{Right}	7	5.00	1.41
MA_{Left}	5	5.40	1.82
CANTAB SWM - Bet Errors			
NC	10	20.84	16.68
MO_{Right}	10	24.60	15.76
MO_{Left}	7	27.33	19.85
MA_{Right}	7	26.50	13.74
MA_{Left}	5	20.00	8.54
CANTAB PAL - Total Errors			
NC	10	8.22	4.09
MO_{Right}	10	17.50	25.69
MO_{Left}	7	6.83	5.84
MA_{Right}	7	9.00	5.72
MA_{Left}	5	6.80	2.49

Note. [1]WMS-III Letter/Number = WMS-III Letter/Number Sequencing Raw Score; CANTAB SWM - Bet Errors = CANTAB Spatial Working Memory – Between Trial Errors; CANTAB PAL - Total Errors = CANTAB Paired Associates Learning – Total Errors.

Table R-6

Means and Standard Deviations for Constructional Abilities

Variable[1]	N	Mean	SD
Rey Figure: Copy			
NC	10	25.15	3.68
MO_{Right}	10	25.55	2.92
MO_{Left}	7	25.36	1.97
MA_{Right}	7	22.93	4.18
MA_{Left}	5	27.20	2.95
Rey Figure: Copy (sec)			
NC	10	213.00	108.46
MO_{Right}	10	178.60	51.09
MO_{Left}	7	213.57	73.90
MA_{Right}	7	147.14	36.89
MA_{Left}	5	197.60	36.75
CANTAB MTS Correct			
NC	10	98.13	2.49
MO_{Right}	10	98.47	2.54
MO_{Left}	7	97.92	1.70
MA_{Right}	7	96.87	3.76
MA_{Left}	5	96.00	2.56
CANTAB MTS Tot Correct			
NC	10	47.10	1.20
MO_{Right}	10	47.20	1.23
MO_{Left}	7	47.00	0.82
MA_{Right}	7	46.50	1.80
MA_{Left}	5	46.08	1.23

Note. [1]Rey Figure: Copy = Rey Figure Copy Score; Rey Figure: Copy (sec) = Rey Figure Copy Time (sec); CANTAB MTS Correct = CANTAB Match to Sample Correct; CANTAB MTS Tot Correct = CANTAB Match to Sample Total Correct.

Table R-7

Means and Standard Deviations for Verbal Expression Measures

Variable	N	Mean	SD
Animal Fluency			
NC	10	20.00	3.40
MO_{Right}	10	19.20	7.33
MO_{Left}	7	20.43	5.44
MA_{Right}	7	15.57	4.08
MA_{Left}	5	21.60	7.37
Food & Drink Fluency			
NC	10	23.80	5.65
MO_{Right}	10	22.40	7.07
MO_{Left}	7	26.00	2.65
MA_{Right}	7	19.86	6.31
MA_{Left}	5	27.20	4.32
Semantic Fluency			
NC	10	43.80	8.38
MO_{Right}	10	41.60	13.14
MO_{Left}	7	46.43	3.87
MA_{Right}	7	35.43	8.81
MA_{Left}	5	48.80	9.34
Letter "S" Fluency			
NC	10	14.30	3.74
MO_{Right}	10	16.00	7.44
MO_{Left}	7	15.14	4.81
MA_{Right}	7	11.86	3.02
MA_{Left}	5	13.60	5.13
Letter "F" Fluency			
NC	10	13.60	3.86
MO_{Right}	10	13.60	4.86
MO_{Left}	7	15.57	5.44
MA_{Right}	7	10.57	2.37
MA_{Left}	5	11.80	4.66
Letter "A" Fluency			
NC	10	12.00	3.74
MO_{Right}	10	9.80	4.26
MO_{Left}	7	12.00	5.29
MA_{Right}	7	7.43	2.37
MA_{Left}	5	8.40	4.88

Table R-7

Means and Standard Deviations for Verbal Expression Measures (continued)

Variable	N	Mean	SD
Phonemic Fluency			
NC	10	39.90	9.34
MO_{Right}	10	39.40	14.68
MO_{Left}	7	42.71	13.16
MA_{Right}	7	29.86	4.88
MA_{Left}	5	33.80	13.41

Table R-8

Means and Standard Deviations for Executive Function Measure

Variable[1]	N	Mean	SD
Stroop Test: Color Word			
NC	10	48.20	11.85
MO_{Right}	10	41.70	8.92
MO_{Left}	7	45.29	11.35
MA_{Right}	7	41.29	5.35
MA_{Left}	5	46.20	8.98
CANTAB ID/ED Stages			
NC	10	8.48	0.82
MO_{Right}	10	8.50	0.71
MO_{Left}	7	7.50	2.57
MA_{Right}	7	8.00	1
MA_{Left}	5	8.84	0.22
CANTAB ID/ED Total Errors			
NC	10	23.08	13.90
MO_{Right}	10	15.90	7.50
MO_{Left}	7	20.67	10.01
MA_{Right}	7	27.50	11.27
MA_{Left}	5	19.60	10.24
CANTAB Sockets of Cambridge Initial Thinking Time (sec)			
NC	10	11.54	6.72
MO_{Right}	10	15.30	9.05
MO_{Left}	7	11.81	6.51
MA_{Right}	7	11.18	15.56
MA_{Left}	5	10.40	5.74
CANTAB Sockets of Cambridge Subsequent Thinking Time (sec)			
NC	10	1.33	1.19
MO_{Right}	10	1.75	0.97
MO_{Left}	7	1.50	1.51
MA_{Right}	7	0.90	0.41
MA_{Left}	5	0.22	0.21
CANTAB Sockets of Cambridge Problems Solved			
NC	10	8.66	1.88
MO_{Right}	10	7.60	0.84
MO_{Left}	7	9.33	1.37
MA_{Right}	7	8.17	1.07
MA_{Left}	5	8.20	2.17

Table R-8

Means and Standard Deviations for Executive Function Measures (continued)

Variable	N	Mean	SD
CANTAB Spatial Working Memory Strategy			
NC	10	29.92	5.80
MO_{Right}	10	32.90	3.48
MO_{Left}	7	34.67	2.21
MA_{Right}	7	33.83	4.06
MA_{Left}	5	28.36	2.23

Note. [1]NC = Normal control subjects; MO_{Right} = patients without aura with right-sided migraine; MO_{Left} = patients without aura with left-sided migraine; MA_{Right} = patients with aura with right-sided migraine; MA_{Left} = patients with aura with left-sided migraine.

Table R-9

Means and Standard Deviations for Motor Function Measures

Variable	N	Mean	SD
Sequential Tapping - Left Hand			
NC	6	122.17	7.88
MO_{Right}	9	102.67	15.65
MO_{Left}	7	115.29	14.28
MA_{Right}	6	109.33	11.43
MA_{Left}	4	113.00	9.80
Sequential Tapping - Right Hand			
NC	6	126.83	21.37
MO_{Right}	9	111.89	16.81
MO_{Left}	7	132.57	17.90
MA_{Right}	6	119.83	9.99
MA_{Left}	4	130.00	28.58
Sequential Tapping - Both Hands			
NC	6	36.92	17.12
MO_{Right}	9	25.56	9.37
MO_{Left}	7	32.71	21.08
MA_{Right}	6	28.08	8.91
MA_{Left}	4	32.75	6.64
Single Tapping - Left Hand			
NC	6	90.33	10.67
MO_{Right}	9	85.22	11.05
MO_{Left}	7	92.57	10.00
MA_{Right}	6	85.50	4.64
MA_{Left}	4	94.25	10.08
Single Tapping - Right Hand			
NC	6	101.00	7.69
MO_{Right}	9	91.56	11.11
MO_{Left}	7	100.00	10.46
MA_{Right}	6	97.00	7.54
MA_{Left}	4	100.25	9.81
Grooved Pegboard - Left Hand			
NC	6	64.25	8.53
MO_{Right}	9	71.17	8.18
MO_{Left}	7	70.64	9.71
MA_{Right}	6	72.67	9.11
MA_{Left}	4	66.75	10.37

Table R-9

Means and Standard Deviations for Motor Function Measures (continued)

Variable	N	Mean	SD
Grooved Pegboard - Right Hand			
NC	6	56.08	6.20
MO_{Right}	9	67.67	8.24
MO_{Left}	7	59.50	7.56
MA_{Right}	6	63.08	4.94
MA_{Left}	4	61.50	9.08
Pinch Strength - Left Hand			
NC	6	17.28	2.70
MO_{Right}	9	14.50	2.12
MO_{Left}	7	15.67	3.11
MA_{Right}	6	13.28	4.47
MA_{Left}	4	12.29	2.87
Pinch Strength - Right Hand			
NC	6	17.28	3.16
MO_{Right}	9	14.86	1.42
MO_{Left}	7	15.71	2.16
MA_{Right}	6	13.28	4.13
MA_{Left}	4	13.79	2.66

APPENDIX S

Non-Significant ANOVA Results for Cognitive and Motor Measures

Table S-1

Attention & Concentration: Non-Significant ANOVA Results

Variable	df	SS	MS	F	p	Power
Digit Span Forward Raw						
Group	4	21.62	5.40	1.84	0.144	0.50
Hemisphere	2	14.61	7.30	2.48	0.098	0.46
Type	2	16.84	8.42	2.86	0.071	0.52
Digit Span Total Score Raw						
Group	4	56.79	14.20	1.24	0.312	0.35
Hemisphere	2	49.82	24.91	2.18	0.129	0.41
Type	2	49.82	24.91	2.18	0.129	0.41
Stroop Test: Colour						
Group	4	363.21	90.80	0.57	0.686	0.17
Hemisphere	2	180.09	90.05	0.57	0.573	0.14
Type	2	305.27	152.64	0.96	0.394	0.20
Stroop Test: Colour Self Corrected Errors						
Group	4	1.86	0.47	1.88	0.137	0.51
Hemisphere	2	0.69	0.35	1.39	0.262	0.28
Type	2	0.79	0.40	1.60	0.217	0.31
Stroop Test: Colour Errors						
Group	4	4.61	1.15	1.27	0.301	0.35
Hemisphere	2	1.66	0.83	0.91	0.410	0.19
Type	2	3.71	1.85	2.04	0.145	0.39
Stroop Test: Word						
Group	4	1579.29	394.82	1.74	0.165	0.47
Hemisphere	2	1094.66	547.33	2.41	0.105	0.45
Type	2	829.78	414.89	1.83	0.177	0.35
Stroop Test: Word Self Corrected Errors						
Group	4	0.98	0.24	3.17	0.026	0.76
Hemisphere	2	0.31	0.16	2.05	0.145	0.39
Type	2	0.32	0.16	2.07	0.142	0.40
Stroop Test: Word Errors						
Group	4	0.10	0.02	0.46	0.764	0.14
Hemisphere	2	0.05	0.03	0.51	0.605	0.13
Type	2	0.05	0.03	0.51	0.605	0.13
Rapid Visual Processing						
Group	4	0.01	0.00	1.01	0.416	0.28
Hemisphere	2	0.00	0.00	1.16	0.325	0.24
Type	2	0.00	0.00	0.52	0.601	0.13

Table S-2

Working Memory: Non-Significant ANOVA Results

Variable	df	SS	MS	F	p	Power
WMS-III: Letter Number						
Group	4	17.99	4.50	0.72	0.586	0.21
Hemisphere	2	14.93	7.47	1.19	0.316	0.24
Type	2	1.11	0.56	0.09	0.915	0.06
Digit Span Backward - Length						
Group	4	13.72	3.43	0.64	0.637	0.19
Hemisphere	2	11.99	6.00	1.12	0.338	0.23
Type	2	8.77	4.39	0.82	0.449	0.18
Digit Span Backward - Raw Score						
Group	4	2.68	0.67	0.32	0.864	0.11
Hemisphere	2	2.65	1.32	0.63	0.540	0.15
Type	2	1.88	0.94	0.45	0.644	0.12
Spatial Working Memory						
Group	4	304.40	76.10	0.30	0.874	0.11
Hemisphere	2	138.12	69.06	0.28	0.761	0.09
Type	2	168.46	84.23	0.34	0.717	0.10
Paired Associate Learning Error						
Group	4	718.87	179.72	0.94	0.454	0.26
Hemisphere	2	323.83	161.91	0.84	0.438	0.18
Type	2	159.31	79.65	0.42	0.663	0.11

Table S-3

Verbal Memory: Non-Significant ANOVA Results

Variable	df	SS	MS	F	p	Power
WMS: Story A Immediate Recall						
Group	4	27.06	6.76	0.51	0.731	0.16
Hemisphere	2	7.83	3.92	0.29	0.748	0.09
Type	2	3.54	1.77	0.13	0.876	0.07
WMS: Story B Immediate Recall						
Group	4	27.75	6.94	0.94	0.455	0.26
Hemisphere	2	27.27	13.64	1.84	0.174	0.36
Type	2	21.51	10.76	1.45	0.249	0.29
WMS: Immediate Recall						
Group	4	14.11	3.53	0.46	0.767	0.14
Hemisphere	2	10.62	5.31	0.69	0.510	0.16
Type	2	10.59	5.29	0.68	0.511	0.16
WMS: Story A Delayed Recall						
Group	4	17.05	4.26	0.41	0.799	0.13
Hemisphere	2	10.28	5.14	0.50	0.613	0.12
Type	2	8.89	4.44	0.43	0.654	0.11
WMS: Story B Delayed Recall						
Group	4	7.96	1.99	0.25	0.910	0.10
Hemisphere	2	6.60	3.30	0.41	0.669	0.11
Type	2	6.64	3.32	0.41	0.667	0.11
WMS: Delayed Recall						
Group	4	8.72	2.18	0.34	0.846	0.12
Hemisphere	2	5.94	2.97	0.47	0.629	0.12
Type	2	7.69	3.84	0.61	0.550	0.14
CVLT-II: Trial 1						
Group	4	11.07	2.77	0.76	0.560	0.22
Hemisphere	2	10.04	5.02	1.37	0.267	0.28
Type	2	6.16	3.08	0.84	0.439	0.18
CVLT-II: Trial 2						
Group	4	17.86	4.46	0.53	0.715	0.16
Hemisphere	2	2.18	1.09	0.13	0.879	0.07
Type	2	14.38	7.19	0.85	0.435	0.18
CVLT-II: Trial 3						
Group	4	2.96	0.74	0.11	0.977	0.07
Hemisphere	2	1.50	0.75	0.11	0.892	0.07
Type	2	0.86	0.43	0.07	0.936	0.06

Table S-3

Verbal Memory: Non-Significant ANOVA Results (continued)

Variable	df	SS	MS	F	p	Power
CVLT-II: Trial 4						
Group	4	21.95	5.49	0.67	0.618	0.20
Hemisphere	2	17.08	8.54	1.04	0.364	0.22
Type	2	10.74	5.37	0.65	0.526	0.15
CVLT-II: Trial 5						
Group	4	32.29	8.07	1.85	0.143	0.50
Hemisphere	2	26.56	13.28	3.04	0.061	0.55
Type	2	17.02	8.51	1.95	0.158	0.38
CVLT-II: Total						
Group	4	321.29	80.32	0.66	0.622	0.19
Hemisphere	2	312.28	156.14	1.29	0.289	0.26
Type	2	181.68	90.84	0.75	0.480	0.17
CVLT-II: Trial B						
Group	4	29.53	7.38	2.00	0.116	0.54
Hemisphere	2	9.26	4.63	1.26	0.298	0.25
Type	2	3.73	1.86	0.51	0.608	0.13
CVLT-II: Immediate Free Recall						
Group	4	62.96	15.74	1.93	0.127	0.52
Hemisphere	2	52.92	26.46	3.25	0.051	0.58
Type	2	51.19	25.59	3.15	0.056	0.57
CVLT-II: Immediate Cued Recall						
Group	4	36.18	9.04	1.31	0.287	0.36
Hemisphere	2	24.67	12.33	1.78	0.184	0.35
Type	2	22.50	11.25	1.62	0.212	0.32
CVLT-II: Delayed Free Recall						
Group	4	71.93	17.98	1.74	0.163	0.48
Hemisphere	2	66.48	33.24	3.22	0.052	0.58
Type	2	48.69	24.35	2.36	0.110	0.44
CVLT-II: Delayed Cued Recall						
Group	4	41.21	10.30	1.33	0.278	0.37
Hemisphere	2	40.91	20.46	2.65	0.085	0.49
Type	2	39.24	19.62	2.54	0.094	0.47

Table S-4

Visuo-Spatial Memory: Non-Significant ANOVA Results

Variable	df	SS	MS	F	p	Power
Rey Figure: Immediate Recall						
Group	4	224.61	56.15	1.77	0.158	0.48
Hemisphere	2	206.81	103.41	3.25	0.051	0.58
Type	2	161.47	80.73	2.54	0.094	0.47
Rey Figure: Delayed Recall Time (sec)						
Group	4	2411.63	602.91	0.69	0.602	0.20
Hemisphere	2	2211.63	1105.81	1.27	0.293	0.26
Type	2	768.29	384.14	0.44	0.646	0.12
WMS-III: Faces I						
Group	4	39.35	9.84	0.63	0.643	0.19
Hemisphere	2	28.66	14.33	0.92	0.408	0.20
Type	2	21.89	10.95	0.70	0.502	0.16
WMS-III: Faces II						
Group	4	37.05	9.26	0.47	0.754	0.15
Hemisphere	2	7.08	3.54	0.18	0.835	0.08
Type	2	34.20	17.10	0.88	0.426	0.19

Table S-5

Verbal Expression: Non-Significant ANOVA Results

Variable	df	SS	MS	F	p	Power
Animal Fluency						
Group	4	137.67	34.42	1.08	0.381	0.30
Hemisphere	2	99.00	49.50	1.56	0.226	0.31
Type	2	13.87	6.94	0.22	0.805	0.08
Animal Perseverations						
Group	4	10.10	2.53	0.86	0.496	0.25
Hemisphere	2	0.15	0.08	0.03	0.975	0.05
Type	2	9.38	4.69	1.60	0.216	0.32
Animal Rule Breaks						
Group	4	0.63	0.16	0.60	0.665	0.18
Hemisphere	2	0.46	0.23	0.87	0.428	0.19
Type	2	0.14	0.07	0.27	0.763	0.09
Food & Drink Fluency						
Group	4	217.93	54.48	1.69	0.174	0.46
Hemisphere	2	205.64	102.82	3.20	0.053	0.57
Type	2	3.19	1.59	0.05	0.952	0.06
Food & Drink Perseverations						
Group	4	3.34	0.84	0.48	0.752	0.15
Hemisphere	2	0.71	0.36	0.20	0.817	0.08
Type	2	2.86	1.43	0.82	0.450	0.18
Food & Drink Rule Breaks						
Group	4	0.30	0.07	0.70	0.596	0.20
Hemisphere	2	0.09	0.05	0.44	0.646	0.12
Type	2	0.09	0.05	0.44	0.646	0.12
Semantic Fluency						
Group	4	676.85	169.21	1.86	0.140	0.51
Hemisphere	2	582.41	291.21	3.20	0.053	0.57
Type	2	27.08	13.54	0.15	0.862	0.07
Letter "S" Fluency						
Group	4	77.96	19.49	0.72	0.586	0.21
Hemisphere	2	1.60	0.80	0.03	0.971	0.05
Type	2	55.26	27.63	1.02	0.372	0.21
Letter "S" Perseverations						
Group	4	2.09	0.52	0.45	0.770	0.14
Hemisphere	2	1.42	0.71	0.61	0.547	0.14
Type	2	1.85	0.93	0.80	0.457	0.18

Table S-5

Verbal Expression: Non-Significant ANOVA Results (continued)

Variable	df	SS	MS	F	p	Power
Letter "S" Rule Breaks						
Group	4	0.35	0.09	0.44	0.779	0.14
Hemisphere	2	0.17	0.08	0.42	0.662	0.11
Type	2	0.19	0.10	0.48	0.621	0.12
Letter "F" Fluency						
Group	4	100.72	25.18	1.33	0.280	0.37
Hemisphere	2	22.82	11.41	0.60	0.554	0.14
Type	2	80.27	40.14	2.12	0.136	0.40
Letter "F" Perseverations						
Group	4	2.35	0.59	0.43	0.789	0.14
Hemisphere	2	0.09	0.05	0.03	0.966	0.05
Type	2	2.14	1.07	0.78	0.468	0.17
Letter "F" Rule Breaks						
Group	4	0.10	0.02	0.46	0.764	0.14
Hemisphere	2	0.05	0.03	0.51	0.605	0.13
Type	2	0.05	0.03	0.51	0.605	0.13
Letter "A" Fluency						
Group	4	126.56	31.64	1.83	0.145	0.50
Hemisphere	2	72.09	36.04	2.09	0.139	0.40
Type	2	101.21	50.60	2.93	0.067	0.53
Letter "A" Perseverations						
Group	4	0.06	0.02	0.02	0.999	0.05
Hemisphere	2	0.04	0.02	0.03	0.971	0.05
Type	2	0.04	0.02	0.03	0.971	0.05
Letter "A" Rule Breaks						
Group	4	0.14	0.04	0.68	0.612	0.20
Hemisphere	2	0.03	0.01	0.28	0.759	0.09
Type	2	0.14	0.07	1.33	0.277	0.27
Phonemic Fluency						
Group	4	759.92	189.98	1.40	0.256	0.39
Hemisphere	2	194.61	97.30	0.72	0.496	0.16
Type	2	634.20	317.10	2.33	0.113	0.44

Table S-6

Constructional Abilities: Non-Significant ANOVA Results

Variable	df	SS	MS	F	p	Power
Rey Figure: Copy						
Group	4	57.46	14.36	1.35	0.272	0.37
Hemisphere	2	28.43	14.22	1.34	0.276	0.27
Type	2	1.18	0.59	0.06	0.946	0.06
Rey Figure: Copy Time (sec)						
Group	4	23615.57	5903.89	1.14	0.353	0.32
Hemisphere	2	20213.58	10106.79	1.96	0.157	0.38
Type	2	9118.73	4559.37	0.88	0.423	0.19
Match to Sample Visual Search - Correct						
Group	4	27.33	6.83	0.96	0.443	0.27
Hemisphere	2	7.62	3.81	0.53	0.591	0.13
Type	2	24.32	12.16	1.70	0.197	0.33
Match to Sample Visual Search - Total Correct						
Group	4	5.82	1.45	0.88	0.485	0.25
Hemisphere	2	1.71	0.86	0.52	0.599	0.13
Type	2	5.31	2.66	1.61	0.214	0.32

Table S-7

Executive Function: Non-Significant ANOVA Results

Variable	df	SS	MS	F	p	Power
Stroop Test: Colour-Word						
Group	4	306.39	76.60	0.80	0.532	0.23
Hemisphere	2	303.76	151.88	1.59	0.219	0.31
Type	2	156.78	78.39	0.82	0.449	0.18
Stroop Test: Colour-Word Self Corrected Errors						
Group	4	8.63	2.16	2.13	0.098	0.57
Hemisphere	2	0.80	0.40	0.40	0.675	0.11
Type	2	6.14	3.07	3.03	0.062	0.55
Stroop Test: Colour-Word Errors						
Group	4	1.24	0.31	0.95	0.448	0.27
Hemisphere	2	0.96	0.48	1.48	0.242	0.29
Type	2	0.81	0.41	1.25	0.300	0.25
Intra/Extradimensional Set Shifting Stages						
Group	4	7.26	1.81	1.10	0.374	0.31
Hemisphere	2	0.55	0.28	0.17	0.846	0.07
Type	2	1.89	0.95	0.57	0.569	0.14
Intra/Extradimensional Set Shifting Errors						
Group	4	608.78	152.19	1.28	0.295	0.36
Hemisphere	2	47.15	23.58	0.20	0.820	0.08
Type	2	239.80	119.90	1.01	0.374	0.21
Tower of London - Initial Thinking Time (sec)						
Group	4	123.98	30.99	0.35	0.840	0.12
Hemisphere	2	36.07	18.03	0.21	0.815	0.08
Type	2	57.56	28.78	0.33	0.723	0.10
Tower of London - Problems Solved with Minimum Moves						
Group	4	13.70	3.42	1.55	0.211	0.43
Hemisphere	2	6.57	3.29	1.48	0.241	0.29
Type	2	1.26	0.63	0.28	0.754	0.09

Table S-8

Motor Abilities: Non-Significant ANOVA Results

Variable	df	SS	MS	F	p	Power
Sequential Tapping Left Hand - Errors						
Group	4	1.42	0.36	0.18	0.946	0.08
Hemisphere	2	0.42	0.21	0.11	0.900	0.06
Type	2	0.60	0.30	0.15	0.858	0.07
Sequential Tapping Right Hand						
Group	4	2096.70	524.17	1.50	0.229	0.40
Hemisphere	2	1520.38	760.19	2.18	0.133	0.41
Type	2	105.43	52.72	0.15	0.860	0.07
Sequential Tapping Right Hand - Errors						
Group	4	4.12	1.03	0.49	0.742	0.15
Hemisphere	2	2.79	1.39	0.67	0.522	0.15
Type	2	3.76	1.88	0.90	0.420	0.19
Tapping Both Hands						
Group	4	556.18	139.05	0.70	0.599	0.20
Hemisphere	2	490.63	245.31	1.24	0.307	0.25
Type	2	268.09	134.04	0.67	0.518	0.15
Tapping Both Hands - Errors						
Group	4	0.45	0.11	0.88	0.490	0.24
Hemisphere	2	0.14	0.07	0.55	0.586	0.13
Type	2	0.16	0.08	0.63	0.540	0.14
Single Tapping Left Hand						
Group	4	412.12	103.03	1.09	0.383	0.29
Hemisphere	2	399.42	199.71	2.11	0.141	0.39
Type	2	11.22	5.61	0.06	0.943	0.06
Single Tapping Right Hand						
Group	4	465.50	116.37	1.25	0.314	0.34
Hemisphere	2	293.11	146.56	1.57	0.226	0.30
Type	2	131.67	65.83	0.71	0.502	0.16
Grooved Pegboard Left Hand						
Group	4	289.93	72.48	0.89	0.484	0.24
Hemisphere	2	255.27	127.64	1.56	0.228	0.30
Type	2	195.14	97.57	1.20	0.318	0.24

Table S-8

Motor Abilities: Non-Significant ANOVA Results (continued)

Variable	df	SS	MS	F	p	Power
Grooved Pegboard Left Hand - Pegs Dropped						
Group	4	0.81	0.20	0.28	0.885	0.10
Hemisphere	2	0.19	0.10	0.14	0.873	0.07
Type	2	0.04	0.02	0.03	0.972	0.05
Grooved Pegboard Right Hand - Pegs Dropped						
Group	4	0.64	0.16	0.33	0.857	0.11
Hemisphere	2	0.62	0.31	0.64	0.536	0.15
Type	2	0.43	0.22	0.44	0.649	0.11

APPENDIX T

Composite Psychological Indices: Means and Standard Deviations and Non-Significant ANOVA Results

Table T-1

Composite Psychological Indices: Means and Standard Deviations

Characteristic[1]	N	Mean	SD
General Cognitive Index			
NC	10	52.54	4.37
MO_{Right}	10	48.44	3.95
MO_{Left}	7	50.18	4.99
MA_{Right}	7	46.63	2.97
MA_{Left}	5	51.27	2.97
Verbal Memory			
NC	10	53.45	6.95
MO_{Right}	10	48.54	7.93
MO_{Left}	7	50.06	9.27
MA_{Right}	7	47.21	5.95
MA_{Left}	5	49.85	4.35
Visuo-Spatial Memory			
NC	10	52.42	5.76
MO_{Right}	10	47.87	5.62
MO_{Left}	7	51.08	6.37
MA_{Right}	7	46.61	3.62
MA_{Left}	5	52.65	4.17
Working Memory			
NC	10	48.7	4.14
MO_{Right}	10	46.46	5.15
MO_{Left}	7	49.97	4.3
MA_{Right}	7	47.05	4.15
MA_{Left}	5	49.3	5.62
Verbal Expression			
NC	10	52.37	4.35
MO_{Right}	10	50.31	9.5
MO_{Left}	7	52.92	4.4
MA_{Right}	7	43.83	3.31
MA_{Left}	5	49.19	5.94
Constructional Abilities			
NC	10	52.46	7.8
MO_{Right}	10	49.84	4.8
MO_{Left}	7	51.03	3.23
MA_{Right}	7	43.48	6.57
MA_{Left}	5	53.09	3.86

Table T-1

Composite Psychological Indices: Means and Standard Deviations (continued)

Characteristic	N	Mean	SD
Attention & Concentration			
NC	10	52.76	6.38
MO_{Right}	10	48.22	4.33
MO_{Left}	7	48.07	4.45
MA_{Right}	7	46.87	4.72
MA_{Left}	5	55.14	4.76
Executive Function			
NC	10	52.01	3.74
MO_{Right}	10	47.05	2.98
MO_{Left}	7	49.02	6.52
MA_{Right}	7	49.92	3.76
MA_{Left}	5	53.36	4.07
Motor Function Right Hand			
NC	6	51.50	4.97
MO_{Right}	9	48.66	3.82
MO_{Left}	7	51.69	3.13
MA_{Right}	6	48.28	5.81
MA_{Left}	4	50.38	2.85
Motor Function Left Hand			
NC	6	52.69	4.07
MO_{Right}	9	47.69	5.47
MO_{Left}	7	52.58	3.29
MA_{Right}	6	48.46	4.83
MA_{Left}	4	48.95	2.69
Emotion & Personality			
NC	10	49.86	3.78
MO_{Right}	10	46.92	6.1
MO_{Left}	7	52.05	3.77
MA_{Right}	7	51.04	3.04
MA_{Left}	5	52.11	3.22

Table T-2

Composite Psychological Indices: Non-Significant ANOVA Results

Composite Index	df	SS	MS	F	p	Power
Working Memory						
Group	4	69.80	17.45	0.81	0.528	0.23
Hemisphere	2	60.77	30.38	1.41	0.258	0.28
Type	2	1.87	0.94	0.04	0.958	0.06
Verbal Memory						
Group	4	194.76	48.69	0.92	0.465	0.26
Hemisphere	2	193.16	96.58	1.82	0.178	0.35
Type	2	151.21	75.61	1.42	0.255	0.28
Verbal Expression						
Group	4	386.74	96.68	2.52	0.059	0.65
Hemisphere	2	206.53	103.26	2.69	0.082	0.50
Type	2	238.88	119.44	3.11	0.058	0.56
Motor Function Right Hand						
Group	4	68.00	17.00	0.93	0.460	0.26
Hemisphere	2	57.89	28.95	1.59	0.223	0.31
Type	2	17.24	8.62	0.47	0.628	0.12
Motor Function Left Hand						
Group	4	156.76	39.19	2.02	0.121	0.53
Hemisphere	2	102.44	51.22	2.63	0.090	0.48
Type	2	58.74	29.37	1.51	0.239	0.29
Emotion & Personality						
Group	4	154.17	38.54	2.03	0.112	0.55
Hemisphere	2	66.93	33.47	1.76	0.187	0.34
Type	2	31.60	15.80	0.83	0.444	0.18