# A Neuropsychological Case Study of Inorganic Mercury Toxicity: Searching for Clinical Characteristics

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**ABSTRACT**

The literature on the effects of mercury poisoning suggests it causes cognitive and psychiatric symptoms. It is suggested that the neurocognitive effects of mercury toxicity include: declines in memory, attention, language and motor function, a no consistent picture emerges. The psychiatric effects of mercury toxicity include nervousness and timidity, shyness, avoidance of people, irritability, noticeable mood changes, depression and anxiety. For this study, a single case of a patient diagnosed with mercury toxicity was conducted in order to obtain an accurate characterisation of the typical neurocognitve picture associated with mercury poisoning. Data was gathered from neuropsychological clinical assessments of the patient conducted over a roughly two year period, along with the patient's medical records. The findings indicate that executive dysfunction was the main neuropsychological characteristic stemming from the patient's mercury toxicity, although this dysexecutive picture was found to largely resolve over the period investigated. During acute stages of mercury toxicity she had memory deficits, poor attention, reduced language ability and motor dysfunction. Her initial presentation also consisted of paranoia, anxiety, depression, psychosis, irritability, aggression, social withdrawal and insomnia. Her constellation of symptoms suggests lesions in the frontal cortex, extending posterially to the perisylvian areas, the basal ganglia and the cerebellum.

Keywords: inorganic mercury toxicity; executive function; frontal lobes; basal ganglia; perisylvian area

## INTRODUCTION

From the 1600s, hatters in the felt hat industry used mercury as a stiffener. The emotional and cognitive changes that hatter's suffered from due to subsequent poisoning may have lead to the term "mad as a hatter" and possibly inspired the "Mad Hatter" in Lewis Carol's *Alice in Wonderland* (Gowdy & Demmers, 1978, as cited in Siblerud 1989; O'Carroll, Masterton, Dougall, Ebmeier, & Goodwin, 1995). In 1860, the first article about mercury poisoning in hatters was published (O'Carroll et al., 1995) and in 1941 it was discovered that the Mad Hatter's Syndrome was due to brain damage caused by mercury toxicity (Gowdy & Demmers, 1978, as cited in Siblerud 1989).

Since then there has been much research to study the effects of mercury on humans. Disasters such as that in Iraq where the consumption of bread made with mercury-treated grain affected thousands in the population prompted some studies (Bakir, Rustham, Tikriti, Al-Damluji, & Shihristani, 1980; Clarkson, 2002). Other studies have focused on individual tragedies. For example, Nierenberg et al. (1998) investigated a chemist who died after dimethylmercury exposure when she accidently dropped a small amount on her hand, which she thought was protected by a latex rubber glove. Studies have also occurred in response to litigation against organisations when employees have suffered due to occupational exposure to mercury (e.g., Powell, 2000).

The description of symptoms is wide-ranging, and includes physical, cognitive, and emotional sequelae. The following aims to accurately describe the neurocognitive features of mercury poisoning.

### Pathology of organic and inorganic mercury poisoning

Although most research in the neuropathology of mercury toxicity has been done with cases of organic mercury poisoning, there is general agreement that both organic and inorganic mercury is particularly harmful to the central nervous system (Clarkson, 2002; Clarkson, Magos, & Myers, 2003; Nierenberg et al., 1998; O'Carroll et al, 1995; Siblerud, 1989). Damage to the brain from mercury poisoning has mainly been studied post mortem (e.g. Nierenberg et al., 1998), and in vivo research with magnetic resonance imaging (MRI) has shown little about the pathological changes in the brain from mercury exposure (e.g. O'Carroll et al., 1995). Nevertheless, findings have been similar across studies. A post mortem analysis of patients who suffered from methylmercury poisoning in Iraq showed that, in general, neuron loss was recorded at all levels of the cortex, cerebellum and cerebrum (Bakir, et al., 1980). The necropsy of a patient, who died in 1957 after exposure to

methylmercury phosphate in 1937, showed similar degeneration in the cerebral and cerebellar cortices (Hunter & Russell, 1954). There was severe atrophy of the area striata, mostly about the calcarine fissures with less damage near the occipital poles. Nierenberg et al. (1998) reported similar findings in a chemist exposed to a few drops of dimethylmercury. They recorded damage in the cerebral cortex, specifically about the calcarine area, and neuronal loss in the cerebellum. Most of the neuronal loss in the chemist was in the visual and auditory cortices; there was less neuronal loss in the motor and sensory cortices. They reported this finding as consistent with two similar cases of exposure to organic mercury, and that in all these cases, mercury concentrations were highest in the frontal lobes. The damage about the calcarine fissures could explain the constriction of the visual fields in patients with mercury toxicity and damage in the cerebellar cortex may explain the ataxia that these patients present with (Hunter & Russell, 1954; Nierenberg et al., 1998). These findings indicate that with respect to the CNS, mercury causes atrophy in the cerebral and cerebellar cortices, and that most damage occurs around the calcarine fissures although mercury levels appear to be highest in the frontal lobes.

In vivo research provides different information about the pathology of mercury poisoning. An MRI scan of a patient who was exposed to phenylmercury ammonium acetate showed tiny lesions in the frontal white matter, with Virchow-Robin spaces in the basal ganglia, whereas no cerebral atrophy was noted. The radiologist described the results as insignificant (O'Carroll et al., 1995). Nierenberg et al. (1998) also recoded insignificant results from MRI scans of their patient on two occasions before her death. However, a single-photon emission computerised tomography scan (SPECT) led to the conclusion that deregulation of the posterior cingulate cortex is a possible consequence of mercury poisoning. The hyperactivity in this area may correlate with the reported attention and concentration deficits and increased anxiety and agitation in mercury exposed patients (O'Carroll et al., 1995). This suggests that mercury poisoning may result in anatomical changes in the brain and also cause dysregulation of neurological activity.

**Inorganic mercury**

Inorganic mercury is used in thermometers and is one of the substances used in dental amalgam (Rossini et al., 2000; Siblerud, 1989; Tang & Li, 2006). The most common passage of inorganic mercury into the blood stream is through the inhalation of mercury vapour, but it can also be ingested orally or absorbed through the skin (Clarkson et al., 2003; Powell 2000; Rossini et al., 2000; Siblerud, 1989). Mercury poisoning causes a combination of cognitive and emotional symptoms, collectively termed erythism (Clarkson et al., 2003; O'Carroll et

al., 1995; Powell 2000). These symptoms have been said to include nervousness and timidity, shyness, avoidance of people, irritability, noticeable mood changes, ataxia, tremors, and weakened intellectual capability (Lishman, 1987, as cited in O'Carroll et al., 1995). Depression, anxiety and insomnia are also reported symptoms of mercury toxicity (Cordeiro Júnior, Faria, & Fráguas Júnior, 2003; Haut, Morrow, Pool, Callahan, Haut, & Franzen 1999).

Research has documented a wide array of cognitive changes resulting from both acute and chronic exposure to inorganic mercury at different levels. Patients exposed to higher levels of inorganic mercury often report memory loss and decreased concentration and attention (Cordeiro Júnior et al., 2003; Powell, 2000; Rossini et al., 2000; Tang & Li, 2006). In testing 13 workers who had been exposed to mercury vapour over two to four weeks, Haut, et al. (1999) found that ten months after exposure the group scored significantly lower than controls for motor skills, visuo-perception, language, speed processing, verbal memory and learning, abstraction and problem-solving. Scores for non-verbal learning and memory and attention were lower than those in the control group but not significantly so. Although the exposed group scored significantly lower for visuo-perception overall, the researchers commented on the lack of significant results for most of the visual perception and construction tests. These findings, along with the lack of significance for non-verbal memory and learning were unexpected, as these are impairments that are frequently reported in the literature (Kishi et al., 1994, Uzzel & Oler, 1986, Vroom & Greer, 1972 and Yeates & Mortensen, 1994 as cited in Haut et al., 1999).

Similar research in a group of Zulu workers previously exposed to mercury in the workplace showed that compared to a control group, the workers scored significantly lower on cognitive tests of sustained and divided attention, but not for executive functioning (Powell, 2000). These findings contradict the Haut et al. (1999) findings, which conclude that mercury exposure predominantly affects executive skills. Conversely, Powell's findings that verbal and spatial memory, motor-speed and manual dexterity were all significantly lower in the exposed group, and that no significant difference was found for visuo-spatial and perception tests, are similar to those of Haut et al. Therefore, it appears as though inorganic mercury at higher levels affects mainly memory and concentration. However, other cognitive domains such as perception, learning, and motor skills may also be affected. It is unclear whether executive functioning is impaired.

Inorganic mercury exposure at higher levels can also disrupt emotional functioning. Depression and anxiety are frequently associated with inorganic mercury toxicity (e.g.

Cordeiro Júnior et al., 2003; Haut et al., 1999; Powell, 2000). Other psychiatric conditions that have been reported include paranoia, psychotic episodes (including hallucinations), and other "peculiar behaviour" (Powell, 2000, Uzzel, 1988). In addition, fatigue, irritability and impaired self-esteem (Rossini et al., 2000). Cordeiro Júnior et al. (2003) report a case study of a 45-year-old male previously exposed to mercury. Following exposure, he developed severe depression, which included social withdrawal, anhedonia, feelings of worthlessness, inappropriate guilt and irritability. These symptoms persisted despite tests showing that no mercury was detectable. However, with treatment on antidepressants his depression was controlled, (O'Carroll et al., 1995). In the literature depression and anxiety are the most commonly reported emotional changes that result from mercury exposure at higher levels. However, the expression of these disorders may vary and may be accompanied by other psychiatric conditions. Furthermore, research suggests that the depression is treatable with medication in mercury-poisoned patients.

Insomnia is also often present in most mercury exposed patients (Rossini et al., 2000). Patients have reported difficulty falling asleep, and experience disrupted sleep. They tend not to remember their dreams or have the sensation of not dreaming; they also suffer from racing thoughts that are part of meaningless dreams. Furthermore, images of persecution and fearful feelings taint the dreams they remember. Other emotional and cognitive and psychological symptoms accompany the insomnia, such as memory loss and depression and agitation (Rossini et al., 2000). Although it is proposed that depressive symptoms can be managed with medication, insomnia and memory loss tend to remain as chronic effects of mercury poisoning (Cordeiro Júnior et al., 2003; O'Carroll et al., 1995; Rossini et al., 2000).

The degree of the symptoms of mercury exposure may be proportional to the level of mercury poisoning. Neurasthenic symptoms; namely headaches, memory loss, dizziness, fatigue, weakness and insomnia and emotional changes such as irritability, mood swings, timidity, nervousness and loss of confidence were found to be present significantly more often in workers tested with mercury toxicity at a urine concentration of $\geq 0.05$ mg/L than workers with lower levels of mercury exposure (Tang & Li, 2006). Other studies have found declines in memory and elevated aggression at low levels of mercury and these declines increase with higher levels of mercury exposure (Echeverria et al., 2005; Ngim et al., 1992) and levels of mercury are proportional to greater mercury blood levels and greater pathological changes (Bakir et al., 1980). Therefore, the literature suggests that higher levels of mercury exposure have greater effects on cognitive and emotional changes (Ngim, 1992; Tang & Li, 2006).

Low levels of mercury may however also have significant effects on cognition. Research has shown cognitive functions, such as visual memory, working memory and attention, verbal memory, motor speed and hand co-ordination, visual scanning and visuomotor co-ordination speed to be significantly reduced by exposure to low levels of mercury (Echeverria et al., 2005; Ngim et al., 1992). Thus, specific areas of cognition, particularly memory, attention, and motor skills can be affected by low levels of mercury.

**Summary**

Much research has aimed at uncovering the effects of mercury on cognition and emotion. However, significant discrepancies exist between findings and further investigation is required in order to construct the complete neurocognitive picture associated with mercury poisoning.

Research needs to distinguish the pathological effects of inorganic mercury on the brain. Additionally, there is need for more in vivo research on the effects of mercury on brain activity. Additional focus on the anatomical and physiological aspects of inorganic mercury poisoning will give greater clarity to why certain domains of cognition and emotion are affected.

There is a need to differentiate between those symptoms that are direct results of mercury damage, and those that result from reactions to the psychological trauma associated with mercury toxicity. For example, depression and anxiety may be reactions to such trauma, an effect of other symptoms such as insomnia, or they could be symptoms that are directly related the effect of mercury on the brain.

Researching the effects of mercury by testing and describing changes in cognition has shown that mercury tends to cause declines in memory, concentration and motors skills at different levels of exposure. However, it is unclear if mercury poisoning causes a decline in executive functioning or not, which, if it does, may cause the other reported damages. Although memory and concentration are most commonly affected, the literature does not specify exactly which parts of memory and concentration are affected, as there are contradictions across different research results. It is possible that memory and concentration difficulties are secondary to executive deficits. Thus, there is no neuropsychologically sophisticated account of what areas of cognition mercury poisoning affects. This is one of the larger gaps in the literature. A similar problem concerns the outlining of the specific effects of mercury on emotional functioning. Moreover, variables other than mercury exposure may confound results that cover emotional disorders in mercury toxic patients. More research is required in order to build a more complete picture of how inorganic mercury specifically

affects cognition and emotion.

In conclusion, despite the broad range of literature covering the effects of mercury on cognition and emotion, there is need for more detailed research. Research needs to target the pathological changes in brain activity and anatomy and specific cognitive and emotional changes that occur with mercury toxicity. This research is aimed at filling in some of the gaps in our knowledge of how cognition and other psychological processes are affected by inorganic mercury toxicity. Instead of focusing on quantification of changes in broad categories of cognition, this study collected detailed qualitative data, based on tests and interviews from a single case study, specifically aimed at refining which areas of cognition are affected. This way, the contradictions in the literature will be somewhat clarified and we will come closer to drawing a much needed description of which areas of cognition mercury poisoning actually effects, and what those effects are.

**Rationale for Research**

Descriptions in authoritative texts, such as *Greenfield's Neuropathology* (Adams & Duchen, 1992) and the *Handbook of Clinical Neurology* (Aminoff, Boller and Swaab, 2008), are sparse and inconsistent. For example, *Greenfield's Neuropathology* describes the clinical features of inorganic mercury poisoning as follows: "Psychological disturbances are the earliest manifestations of mercury poisoning, consisting of emotional lability, depression, outbursts of anger and insomnia. This syndrome is known as erythism. A course tremor develops if exposure continues." (Adams & Duchen, 1992, p. 897). The *Handbook of Clinical Neurology* is even sparser in its description and is quite different from the *Greenfield's Neuropathology* description: "...chronic exposure to mercury also produces personality change and dementia ...Victims developed severe and uncontrollable muscular tremors and twitching limbs known as "hatter's shakes". Other symptoms included hallucinations, impaired vision, and confusion." (Saxton & Morrow, 2008, p. 854). Thus, there is clearly a need for a more precise description of the neuropsychological presentation of mercury poisoning in humans.

Poor clinical characteristics are problematic for practical reasons. Firstly, it is difficult to conduct a clinical assessment without clear guidelines of what to look for and what to expect. People that have had exposure to mercury need correct assessment in order to receive the right medical treatment and advice. Having a set of accurate clinical characteristics will assist medical practitioners to gauge mercury toxicity in their patients efficiently and correctly. Having a set of clinical characteristics may also enable practitioners to provide a more accurate prognosis to their patients. As mercury poisoning can have life changing

effects, knowing what to expect may help those suffering from mercury toxicity to adapt and come to terms with related disabilities and lifestyle changes.

Secondly, clinical characteristics will enable investigations for litigation purposes to be more efficient. One of the more common places for inorganic mercury exposure is in industrial settings where mercury is used (e.g.; Haut et al., 1999; Powell, 2000). Mercury toxicity can be so debilitating that sufferers of the condition can no longer work (e.g., Powel, 2000; Rossini et al., 2000). Death can also result from exposure to mercury (e.g., Nierenberg et al., 1998; Powell, 2000). Employees and the families of employees who are now disabled or dead because of exposure to mercury in their work place, through no fault of their own, should be able to claim for damages from the industry and to apply for disability grants. This may be particularly poignant in situations where industries have not educated their employees about the hazards of mercury and mercury vapour and have not invested in and enforced safety protocols and procedures. An example of such a case occurred in a South African Thermometer processing plant (Powell, 2000). A set of clinical characteristics will protect both employees and employers from unjust litigation outcomes and may enable faster litigation procedures.

## AIM

The review of literature shows that mercury is know to poison the CNS, and that there is some overlap in the literature regarding the reported effects of mercury poisoning on cognition and other psychological processes. Therefore, it is hypothesized that there is a typical neuropsychological characterisation of mercury poisoning. The aim of the research is to accurately characterise and document the neuropsychological sequelae of mercury poisoning in a single case. This contribution can thereby contribute towards solving the current lack of understanding as to what to expect neurocognitive in such cases

## METHODOLOGY

### Sample

The single case study was of a patient previously diagnosed with inorganic mercury toxicity. She was referred from Groote Schuur Hospital to the Neuropsychology Department at the University of Cape Town (UCT) with request to conduct a neurocognitive assessment. Because of the rarity of mercury exposed patients, our sample size of one was determined by the practical constraint of limited potential participant's. However, this benefited the research because it enabled a detailed qualitative investigation to be conducted. The sampling procedure was random, whereby any potential participants with a confirmed diagnosis of mercury toxicity, that were over 18 years old and that had previously been referred to the UCT Neuropsychology Department were contacted by email. We were only able to qualify one patient, Ms X, for this research. She was a Black, 26 year old female. She was fluent in English and highly educated and evidently of with high functional capacity, as she was currently completing her PhD at the time of her mercury exposure.

### M**aterials**

*Primary assessment:*

The materials used in this case included: a review of the patient's medical history taken from the referring doctor, patient hospital folder records, the results of neuropsychological tests performed on the patient and a semi-structured interview with the patient.

The following neurocognitive tests where used to assess the patient:

In order to assess short-term verbal memory, the *Digit Span Test*, a subtest from the *Wechsler Adult Intelligence Scale – Revised* (WAIS –R, Wechsler, 1987) was used. This test comprises a series of sequences of random numbers, with each trial increasing in length from three digits to eight, which the patient is required to repeat back when administered one line

at a time. For the assessment of visual short term memory, the *Spatial Span Test*, also a subtest from the *Wechsler Adult Intelligence Scale – Revised* (WAIS –R, Wechsler, 1987): Here, a series of blocks are pointed to at a rate of one block per second, with the patient being required to point to the same blocks in their order of presentation.

For the assessment of verbal memory, the *Babcock Story Recall Test* (Babcock and Levy, 1940) was administered. Here, the patient is asked to recall the story read by the neuropsychologist immediately after it has been completed. Hereafter the story is read of a second time and the patient is again asked to recall it. The story is made up of 21 scored units of information. When used qualitatively, the way the patient structures their recalled account, and whether they benefit from prompting, can both be used as indicators of executive impairment.

The assessment of visuo-spatial perception involved the use of *Benton's Judgement of Line Orientation Test* (Benton, Sivan, Hamsher, Varney, & Spreen, 1994). This test requires the patient to judge the orientation of two lines, placed in various configurations across items, in relation to a set of numbered lines depicted in a semi-circular shape. The patient is required to identify the numbers of the lines that correspond with the correct orientation of the lines provided in each stimulus item.

For the assessment of language function and higher visual perception, this case drew on the *Boston Naming Test (BNT)*, a subtest from the *Boston Diagnostic Aphasia Examination* (BDAE - 3, Kaplan, Goodglass, & Weintraub, 1983). For this test, the patient is presented with sixty line drawings, which require to be correctly named. This tests naming ability and higher visual perception, including visual gnosis.

Three primary measures of executive function were used in this study. Firstly, the *Rey Complex Figure Test* (Meyers & Meyers, 1955b) was utilised. Here, the patient has to copy a picture of a meaningless complex figure, and is then asked to redraw the picture from memory without being forewarned when it is first presented that it is a memory test that requires remembering. This test has multiple roles in assessment and is used to test visuo-spatial constructional ability, visual memory, neglect and executive functioning (ability to plan and cope with complexity).

Secondly, the *Colour – Word Inference Test* was chosen. This is a subtest from the *Delis-Kaplan Executive Functioning Scale* (D-KEFS, Delis, Kaplan & Kramer, 2001). The patient is presented with a list of words of the colours red, blue and green. The ink colour of each word is red, blue or green, and different to the meaning of the written word. Depending on which card is presented, along with varying instructions, the patient is required to read

either the word or state the colour of the word. This test primarily assesses the patient's ability to inhibit habitual responses, and demonstrates whether he/she has set changing ability.

Thirdly, the *Twenty Questions Test* was incorporated into this study as a measure of the patient's ability to think abstractly and demonstrate cognitive flexibility. This is also a subtest from the *D-KEFS* (Delis, et al., 2001). The patient was required to identify which picture from a sheet of images the assessor was thinking about by asking as few "yes" and "no" questions as possible.

*Tests used for the previous assessments of patient:*

In addition to the tests listed above, the other tests previously done on the patient, used for the tentative comparisons of here neurocognitive state over time include the following. Firstly, *Digit Span (backwards) Test,* a subtest from the *Wechsler Adult Intelligence Scale – Revised* (WAIS –R, Wechsler, 1987) was used to assess working memory. Secondly, the *Controlled oral Word Association: FAS Test* (COWAT: FAS, Benton & Hamsher, 1989) was used as a test of executive functioning, specifically generatively. Thirdly, the *Trail Making Test (TMT)* was also used as a test of executive functioning. This is a subtest from the *Delis-Kaplan Executive Functioning Scale* (D-KEFS, Delis, Kaplan & Kramer, 2001). Fourthly, the *Grooved Peg Board Test* (Mathews & Kløve, 1964) was used as a test for motor dexterity/psychomotor functioning. And finally, the *Cube Analysis Test,* a subtest from the *Visual Object and Space Perception Battery* (VOSP, Warrington & James, 1991) was utilised to assess the patient's spatial perception. This test comprises 14 items in the form of two-dimensional drawings of three-dimensional piles of blocks. In some instances some of the blocks hidden from view. The patient is asked to count how many blocks constitute each item of each of the 14 items.

**Design**

A case study design involving a single case was adopted for this research for two primary reasons: firstly, to allow for one in-depth neurocognitive examination to take place, and secondly, due to the scarcity of mercury poisoning cases in the Western Cape. The case study approach enables one to gain a complex and comprehensive set of data covering a large range of descriptive characteristics about the effects of mercury toxicity. This study draws upon the hypothetico-deductive clinical approach in analysing the patient's neurocognitive test performance, focusing on qualitatively interpreting the test scores (descriptive statistics) in a neuroanatomically meaningful manner. In addition to the tests scores, the overall neurocognitive presentation of the patient is also evaluated in the light of patient and her

medical history. Therefore, for this design the converging lines of evidence draw upon: an open-ended interview and history taking, an examination of the patient's medical records, neurocognitive testing, and careful observation of the patient. The individual tests used for the neurocognitive testing were chosen because they are well established, are recognized to have satisfactory validity and reliability (Lezak, Howieson and Loring, 2004; Strauss, Sherman, & Spreen, 2006). Furthermore, they are used in the everyday clinical practice of the neuropsychologists working at Groote Schuur Hospital.

Along with the data gathered from this primary assessment for the central aim of characterising the neurocognitive picture associated with mercury poisoning, a secondary comparison with the same patient's results from previous neuropsychological assessments was also made. This latter comparison was made possible because this patient had been assessed in a similar manner on two separate occasions by another neuropsychologist — this was only discovered after her assessment had taken place. The patient was first assessed in February 2008, one month after her last exposure to inorganic mercury. She was reassessed six months later in August 2009. Our research assessment took place 13 months after her last neuropsychological assessment and about 19 months since her last exposure to inorganic mercury, on the 29th September 2010. This additional aspect of the research design allowed for a tentative look at potential neurocognitive changes over time in mercury poisoning.

**Data Analysis**

The data analysis for this study incorporated both qualitative and quantitative approaches. The qualitative data gathered included the case history in the form of a detailed open-ended interview, the careful clinical observation of the patient's behaviour, the review of the patient's medical records, and finally the clinical interpretation of her test performances. The quantitative aspects of the data analyse involved the use of descriptive statistics to meaningfully interpret each individual test performance. The test results, together with the findings from the interview and observations noted during the assessment, were analysed in the light of established clinico-pathological correlations.

**Procedure**

This research has adhered to the ethical guidelines and received ethics approval from both the University of Cape Town Department of Psychology Research Ethics Committee and the University of Cape Town Faculty of Health Sciences Research Ethics Committee (Appendix 1). The selected patient was contacted telephonically and a suitable time for the assessment was arranged. She was ensured that a decision not to partake in the research would not affect her treatment in any way, her participation was completely voluntary, and

should she choose to participate she had the right to withdraw from the research at any time without suffering any repercussions. In order to give her time to consider her participation in the study and to discuss it with family and friends, we provided her with the relevant information about the research and the planned assessment with no information being intentionally withheld. This was a minimal risk study, but we disclosed any risks and benefits and provided the patient with an information sheet about the study (Appendix 2).

Written, informed consent from the patient was required before the assessment began (Appendix 2). We provided the patient with all the relevant information about the assessment procedure and the research for which we were collecting data. She was informed about what was to be expected during the assessment and we made sure she was aware of the right to withdraw from the study at any point.

The neuropsychological assessment took place at Groote Schuur Hospital, using the hospital facilities. The assessment was conducted by myself and Professor Mark Solms, a neuropsychologist. The setting for the assessment was organised in such a way as to provide optimal testing conditions for the patient. Following Lezak et al. (2004) suggested conditions for neuropsychological assessment, we ensured the setting was not intimidating for the patient and did not cause her emotional discomfort. The assessment setting was private and free from distractions. Throughout the assessment, the patient was monitored for mental or physical fatigue or tiredness. Finally the patient was debriefed and any questions and concerns that she had not raised during the assessment were encouraged and answered.

The first stage of the assessment was an open-ended, semi-structured interview that provided an in-depth exploration of the patient's experience of cognitive and psychological changes since exposure to mercury, as well as other related physiological changes. We noted the route of exposure and the length and level of exposure from both the medical report and from self-report of the patient. According to Morrow, Muldoon, and Sandstorm (2001), toxicity covaries with the dose and different levels of exposure will determine the effects in the exposed organism. Thus, we consider the level of mercury exposure and the duration of exposure as important variables. We recorded subject variables such as age, sex, general health status, and socio-economic status. The research findings also relate to the patient's medical history. This information was necessary because variables such as age, genetic factors, sex, and health status, can mediate the toxic effects of a chemical (Morrow et al., 2001). Other subject variables such as a certain level of education, social history and preferred language, can affect the patients competency in completing or understanding neuropsychological tests, thus confounding results. By recording these details and taking

them into account, we could better interpret test results. We carefully monitored any other patient variables, such as stress due to examination or being in a hospital setting that may have affected the patient's test performance and results. The interview took about 1 hour.

The second stage of the assessment involved conducting several typical standard neurocognitive tests to assess the level of the patient's cognitive functioning against her previous neurocognitive test scores. The cognitive domains that were considered for this assessment were 1) orientation and attention, 2) memory, 3) language, 4) spatial cognition, 5) motor function and 6) executive function.

## RESULTS

### Case History

Ms X, a 26 year old female fluent in English, was referred to Groote Schuur Hospital for mercury poisoning. She is an organic chemist and at the time of mercury exposure she was completing her PhD in organic chemistry. Her thesis involved making mercury amalgams, and in conducting her research she was exposed to inorganic mercury vapour between early 2008 and January 2009. She first started noticing symptoms, such as her hair falling out and persistent insomnia, from August 2008. By October 2008 she was experiencing a multitude of symptoms and suspected she had mercury poisoning. She had her blood tested towards December 2008. The first set of tests was invalid due to testing errors; she then had urine samples taken. However, she had already ceased working with mercury for a month when urine samples were taken and it is suspected that her mercury levels had declined by this stage. Nevertheless, urine samples showed her mercury levels were still high on the 2$^{nd}$ February 2009, at 20. 71 µg / g creatinine. By the 24$^{th}$ February 2009, her mercury levels had decreased to 4.77µg / g creatinine.

Ms X had been consistently exposed to mercury in her workplace. Her office was in the same room as the hood in which mercury amalgams were made. When the room was assessed, it was found that mercury vapour was escaping from the hood and into the office which was not well ventilated. Mercury had settled in the paint and other surfaces in the office over time. Ms X was originally making one amalgam a day; however, she started to make two a day in order to assist a colleague. Despite the protection of the hood she was still in contact with the mercury vapour which would escape. She also mentioned that she would spend a lot of time in a dark room with the prepared amalgam and that, when assessed, this room was also said to be contaminated with mercury vapour.

At the onset of the initial symptoms Ms X consulted the hospital's Hepatology

Department. Blood tests revealed that she was mildly anaemic and she was subsequently started on a course of iron and multivitamins. However, the symptoms persisted, diversified and increased. She consulted a medical doctor because she had an itchy scalp and her hair was falling out. He diagnosed her with alopecia but was not sure of the cause. By October 2008 she was suffering from a range of physical, cognitive and psychiatric symptoms. She consulted the Dermatology Department because her hair was very brittle and falling out, her nails were breaking, and she had a noticeable skin rash on her face and the skin on her hands was peeling. She had started writing down her symptoms and suggested to them that she should be checked for mercury toxicity. The diagnosis was confirmed a few months later after her urine samples came back. She did not receive any medical treatment for the mercury toxicity but was advised to avoid any further contact with the toxin, which she did from January 2009. Her first neuropsychological assessment was conducted on 12 February 2009, by which stage she was already out of the acute phase of mercury toxicity; however a second assessment six months later, on 7 August, revealed subsequent improvement and suggested that she had in fact been suffering more severe effects of mercury poisoning on her first assessment despite scoring within a normal range in cognitive tests.

Prior to mercury exposure the patient was of good health and had no psychological or medical complaints.

**Symptoms from Self Report, guided questioning and medical records**

Physical symptoms initially included brittle hair and hair loss, an itchy scalp, breaking nails, a skin rash on her face and the skin peeling off her hands. She also developed a persistent cough, her gums would bleed, and she was salivating more than normal. She was very weak and tired, and suffered from persistent insomnia. She developed a resting tremor in her hands, her dexterity declined and she suffered from dysmetria as well as a vestibular "wooziness" after swimming. She would have panic attacks due to paranoid thought processes and would react to imagined danger with a full physiological response where her heart rate increased and she would have sweaty palms. Her appetite was unaffected.

Her psychiatric symptoms included paranoia, anxiety and depression. She would suffer from repetitive, racing thoughts at night, which she described as self critical and paranoid. It is possible that she suffered from auditory hallucinations as she said she could hear this voice speaking out her thoughts. She could not calm herself down and felt like a different person. If she was able to fall asleep her thoughts would continue into her dreams and she would have nightmares that were of similar content to her paranoid thoughts during the day. They would disturb her sleep and wake her up. She could not always differentiate

between her thoughts and her dreams.

She became anti-social, withdrawn and paranoid. She would often have panic attacks and run away in fear if someone looked at her or moved too fast. She was convinced that people were going to shoot her. She also suffered from religious fears and disillusionments. She became very irritable and more aggressive. She was a volunteer at a children institution but had to resign as she could not handle the children patiently. She became un-empathetic to them and was more likely to use physical force when dealing with their disputes which she disclosed as not being in her nature. In the most recent assessment, she described herself as very empathetic, patient and gentle prior to the mercury exposure. She became mildly depressed during this time.

Neurocognitive symptoms included declined memory and attention, language difficulties, reduced praxis and spatial difficulties, poor visuo-motor co-ordination and reduced executive function. She experienced forgetfulness in a multitude of ways. For example, she would read a scholarly article and then completely forget she had read it, often re-ordering articles and only discovering she already had them when filing them electronically. On a few occasions she would not have any recollection of certain events, such as going to the laboratory. Although her perception was unaffected and she could recognise faces, she would forget how she knew people. All this suggests dysfunction of declarative memory, including her episodic memory. Her non-declarative memory was also affected as she would forget previously automatic procedures. For example, she would need to look up recipes to bake a simple cake, whereas these procedures where automatic prior to mercury exposure. She had enormous difficulty in learning to drive and eventually gave up the activity. Additionally she suffered from everyday forgetfulness and disorganisation which suggests a decline in her executive functioning; this was confirmed in her initial neuropsychological assessments as her working memory scores were considered low for someone of her education and previous ability.

She had mild anomia and alienation of word meaning, and she would forget how to spell simple words, such as “couch”. Her semantic knowledge and verbal fluency were both negatively affected. The reports from her initial assessments described her as having difficulty with attending to the task at hand during the tests. She lost her way in familiar places on a couple of occasions; this was due to inattention and not to a perceptual dysfunction. Her spatial attention declined and she would misjudge distances, drop objects and bump into things. She did not have any left neglect or suffer from somatoparaphrenia, apart from one occasion where she lost the ability to move her left arm and had slurred

speech and; this was followed by searing pain and a rush of pins and needles down her arm and into her hand. Her arm looked "plastic" to her and felt weak for hours after the experience. It is thought that this may be due to a simple partial seizure. However, her MRI scans, EEG and ECG came back normal.

She displayed ideational apraxia and was unable to complete certain tasks effectively, such as drive or carry out relatively simple procedures. She would frequently bump her head when disembarking from public transport and couldn't accurately interact with her surroundings, this was complicated by dysmetria.

Her ability to calculate was unaffected as was her visual and colour perception. She could not comment on any change in her handwriting as she tends to type. She did not recall having difficulty with recognition of places and people.

**Present symptoms**

Ms X has not been in contact with mercury for nearly two years. She describes her health as back to normal. She is no longer suffering from any physical symptoms and is unaware of residual cognitive difficulties. Her psychiatric symptoms have also subsided; however, she still suffers from occasional panic attacks and feels hypervigilant around strangers. This is currently being successfully treated with Valarian, a mild tranquiliser, which manages her anxiety and nervous tension.

**Neurocognitive Testing**

The results from the neurocognitive testing are presented in Table 1.

For the first assessment Ms X's short-term verbal memory, as assessed the *Digit Span (forwards Test)*, was scored at five. She scored six on both the second and third assessments. On the *Spatial Span Test*, she scored five for the first and second assessments and six for the third assessment.

On assessment of verbal memory, using the *Babcock Story*, Ms X scored 13 out of 21 for the immediate recall and 15 for both the second and third recalls during the first assessment. When she was assessed six months later, she scored 10, 13 and 12 respectively. For the third assessment she scored 15 on the immediate recall trial and 17 for the second trial. A third trial was not done due to time constraints.

For the assessment of language function and higher visual perception, using the *Boston Naming Test (BNT)*, Ms X scored 46 out of 60 for the third assessment (only a qualitative impression was provided for the first two assessments). No abnormalities of visual perception were noted.

For the assessment of visuo-spatial function, using the *Judgement of Line Test*, Ms X

scored 24 out of 30.

Three primary measures of executive function were used in this study using the *Rey Complex Figure Test*, the *Colour – Word Inference Test and* the *Twenty Questions Test*. On the *Rey Complex figure Test*, Ms X score 35 out of 36 for copy trial during her first assessment, and 15 for both the immediate recall and delayed trials. For the second assessment, she scored 34, 22 and 20 respectively. Finally, for her third assessment she scored 32 and 31 the copy and the immediate recall. A delayed recall was not done.

When assessed using conditions three and four of the *Colour – Word Inference Test*, Ms X took 96 seconds with three self corrected errors for condition three and 87 seconds with two self corrected errors on condition four, on her first assessment. For her second assessment six months later, she took 57 seconds with two self corrected errors and 70 seconds with no self corrected errors, respectively. Finally, for her third assessment, she took 35 second with two self corrected errors and 80 seconds with three self corrected errors respectively.

Five trials of the *Twenty Questions Test* were administered. Despite this, Ms X was only to correctly answer the first trial, which was as a result of guessing. This took 90 seconds. For the remaining trials, there was evidently a misunderstanding between the examiner and Ms X with regard to a difference in classification of the categories of items (e.g.; what constitutes and animate and inanimate objects).

*Tests only used for the previous assessments:*

For the *Digit Span (backwards) Test*, Ms X scored five for the first assessment and five again six months later.

On the *COWAT: FAS Test* she scored 10 for “F”, 10 for “A” and 17 for “S”. Six months later she scored 14, 12 and 10 respectively.

For the *Trail Making Test*, conditions two, three and four were administered. On the first assessment, Ms X took 20.5 seconds for condition two, 51.4 seconds for condition three and 82.4 seconds for condition four. Six months later she scored 21.6 seconds. 36.7 seconds and 79.7 seconds, respectively.

On the *Grooved Peg Board Test*, Ms X initially took 65 seconds, with one error for the left hand and 76 seconds with one error for the right hand. At the second assessment she took 66 seconds with no errors for the left hand, and 79 seconds with one error for the right hand.

Finally, for the *Cube Analysis Test*, she scored 12 out of 14 during the first assessment, and 13 out of 14 six months later.

Table 1.

*Raw neurocognitive test scores over three separate assessments*

| Test | 11/02/2009 | 03/08/2009 | 28/09/2010 |
|---|---|---|---|
| **Working Memory** | | | |
| *Digit Span* [a] | | | |
| Forward | 5 | 6 | 6 |
| Backward | 5 | 5 | • |
| *Spatial Span* [b] | 5 | 5 | 6 |
| **Long-term Verbal Memory** | | | |
| *Babcock Story* [c] | | | |
| 1st Recall | 13 | 10 | 15 |
| 2nd Recall | 15 | 13 | 17 |
| Delayed Recall | 15 | 12 | • |
| **Language** | | | |
| *Boston Naming* | Slightly slow, a few end ones incorrect | Faster but made similar mistakes | 46/60 items correct, fair speed but below what is expected |
| **Executive Function** | | | |
| *Rey's Complex Figure* [d] | | | |
| Copy | 35 | 34 | 32 |
| Immediate Recall | 25 | 22 | 21 |
| Delayed Recall | 15 | 20 | • |
| *Colour – Word Inference Test* [e] | | | |
| 3rd Condition | 96(3) | 57(2) | 35(2) |
| 4th Condition | 87(2) | 70(0) | 80(3) |

(continued)

| Test* | 11/02/2009 | 03/08/2009 | 28/09/2010 |
|---|---|---|---|

| | | | |
|---|---|---|---|
| *Twenty Questions* | • | • | 90 seconds on first trial. Other four trials terminated due to misinterpretation of item classification |
| *COWAT: FAS Test* [f] | | | |
| "F" | 10 | 14 | • |
| "A" | 10 | 12 | • |
| "S" | 17 | 10 | • |
| *Trail Making Test* [g] | | | |
| 2nd Condition | 20.5 | 21.6 | • |
| 3rd Condition | 51.4 | 36.7 | • |
| 4th Condition | 82.4 | 79.7 | • |
| **Psychomotor functioning** | | | |
| *Grooved Peg Board Test* [h] | | | |
| Left hand | 65(1) | 66(0) | • |
| Right hand | 76(1) | 79(1) | • |
| **Spatial perception** | | | |
| *Judgement of Line Test* [i] | • | • | 24 |
| *Cube Analysis Test* [j] | 12 | 13 | • |

Note. • = No test was conducted.

[a] Length of recalled verbal span in units of one. [b] Length of recalled visual span in units of one. [c] Score out of 21. [d] Score out of 36. [e] Time in second (number of self corrected errors). [f] Number of words. [g] Time in seconds. [h] Time in seconds (number of errors). [i] Score out of 39. [j] Score out of 14.

## DISCUSSION

A review of the case of Ms X shows how exposure to inorganic mercury initially caused a number of physical, psychiatric and neurocognitive symptoms. Ms X first presented with psychiatric symptoms including, paranoia, irritability, aggression, insomnia, auditory hallucinations, anxiety, depression and social withdrawal. Neurocognitively, she suffered predominantly from moderate declines in executive function and working memory, attention and long-term visual memory. Her self- report suggested she suffered declined motor ability and spatial dysfunction and language dysfunction. Despite the apparent extensive effects of mercury toxicity, the converging lines of evidence suggest that a moderate dysexecutive syndrome is the main dysfunction in this case. This dysfunction can explain the array of cognitive and psychiatric symptoms see with Ms X. The improvement in her neurocognitive performance over a nearly two year period and self-reported feelings of returning to health suggest that, despite the disability she experienced during the acute and post-acute stages of mercury toxicity, the damage done by mercury toxicity can in fact resolve over time.

Although Ms X's test performances by the time of her third assessment were not indicative of significant neurocognitive impairment, her performance was still imperfect considering her high level of functioning.

An analysis of her overall results shows that her main areas of poor performance where with respect to working memory, problems with generativity, and with abstract reasoning, although all these domains seemed to improve over time. For example, her first assessment times were slow for the *Colour – Word Inference Test* were 96 seconds with three self corrected errors for condition three and 87 seconds with two self corrected errors on condition four, and for the *Trail Making Test*, conditions two, three and four, she took 20.5 seconds, 51.4 seconds and 82.4 seconds respectively, indicated some executive dysfunction. Her poor working memory performance (a backwards digit span score of five initially) was also indicative of executive impairment. Furthermore, qualitatively her test performance for the *Colour – Word Inference Test* is describes her to have shown difficulty with task switching. In the follow up assessments her times for the *Colour – Word Inference Test* improved to 57 seconds with two self corrected errors for condition three on the second assessment and 35 seconds with two self corrected errors on the third assessment. For condition four her times were 70 seconds with no self corrected errors and 80 seconds with three self corrected errors respectively. Again, these scores are within normal limits but are low considering what is expected of Ms X. This and her difficulties with the *Twenty Questions Test* in the third assessment suggest she is still suffering from some mild executive

dysfunction. Finally, her performances on the *FAS test* over the first two assessments reveal a problem with generativity, consistent with the rest of her executive performances at that time.

The improvement in her performances over time highlight how, during the acute phases of mercury toxicity, she suffered from a moderate dysexecutive syndrome. From her self-report it is clear that she also battled with self regulation, as she stated that she had slowness in her activities and speech, and an "everyday forgetfulness" during the acute stages of toxicity. From this it is clear that mercury toxicity have a significantly harmful effect on executive functioning.

Ms X's neurocognitive picture was not entirely consistent with the literature; however, there are still a number of similarities. She presented with mild motor dysfunction. She developed a resting tremor, had ideational apraxia, difficulty interacting with her environment as she could not effectively co-ordinate herself spatially and suffered from dysmetria. Clumsiness, ataxia, tremors and reduced fine movement dexterity are all mentioned as results of mercury toxicity; however apraxia is not specifically mentioned (Echeverria et al., 2005; Haut et al., 1999; Hunter & Russell, 1954; Ngim et al., 1992; Nierenberg et al., 1998; Powell, 2000). These symptoms, in combination with her difficulty with procedural learning suggest dysfunction in the basal ganglia and cerebellum. Cerebellar atrophy is recorded in literature more commonly than lesions in the basal ganglia (Hunter & Russell, 1954; Nierenberg et al., 1998; O'Carroll et al., 1995). Cerebellar damage, explains Ms X's poor motor-spatial judgement and vestibular wooziness. However, her resting tremor, apraxia and difficulties with procedural tasks are most attributable to lesions in fronto-parietal cortex and the basal ganglia. Her MRI scan and ECG were reported to be normal, but it is possible that MRI scans are ineffective at detecting lesions in mercury toxicity cases, as even in the most severe and fatal cases, MRI scans are recorded as insignificant in the literature (Nierenberg et al., 1998; O'Carroll et al., 1995).

Ms X suffered from an initial self-reported decline in declarative memory, phases of episodic amnesia and reduced non-declarative memory particularly when trying to recall previously automated procedures. Episodic and procedural memory loss are not commonly pin-pointed as symptomatic of mercury poisoned patients, but patients do complain of general memory loss and difficulty with everyday activities (Cordeiro Júnior et al., 2003; Powell, 2000; Rossini et al., 2000; Tang & Li, 2006). Her tendency to become lost in familiar places, during the acute phase of mercury toxicity, suggests that perhaps her spatial memory and attention were also affected, but these symptoms could be attributed to executive dysfunction. Executive dysfunction explains most of her other her other deficits in cognition

as well as her inability to contain limbic activity in a rational manner. Visual memory, working memory and attention, verbal memory, spatial memory and learning are all known to be reduced in patients exposed to mercury at both low and high levels of exposure (Echeverria et al., 2005; Haut et al., 1999; Ngim et al., 1992; Powell, 2000). However, the literature is inconsistent with regard to the effect of mercury toxicity on executive function, as certain reports claim it is unaffected (e.g.; Powell, 2000) while others claim otherwise (e.g.; Haut et al., 1999). Nevertheless, the literature documents the highest concentration of mercury levels to be found within the frontal lobes, which regulate executive functioning, of deceased mercury poisoned patients (Hunter & Russell, 1954; Nierenberg et al., 1998; O'Carroll et al., 1995, Ward, 2006). From the clinical picture of mercury poisoning that this research has accumulated, we conclude that executive dysfunction and thus lesions in the frontal lobes are, in fact, a major contribution to the clinical picture of mercury toxicity in human adults.

The general trend in Ms X's scores show a more marked improvement in the first six months of detoxification, with a less striking improvement over the following 13 months. There is a question as to whether we are seeing Ms X's final neurocognitive state as we approach the two year mark since she suffered the acute stages of inorganic mercury toxicity (i.e. the two year time frame that clinicians use to assess spontaneous recovery). The question of whether mercury toxicity follows the same rule of thumb of spontaneous recovery that traumatic brain injury follows arises from this discovery.

As her perception and sensation were not affected, it is unlikely that there was significant damage to occipital areas of the cerebral cortex.

One of the first symptoms the patient in our research suffered from was insomnia. Insomnia is frequently reported as an early complaint by mercury exposed patients and the description Ms X provided of her insomnia was very similar to other cases in the literature(Cordeiro Júnior et al., 2003; Powell, 2000: Rossini et al., 2000). Despite being constantly tired and weak, she could not sleep or remain asleep because she experienced racing thoughts at night or had disturbing dreams which woke her. This too has been described by other patients with mercury toxicity (Rossini, et al., 2000). The content of her dreams runs parallel to other cases as they shared a theme of being nightmarish and terrible, representing thoughts of paranoia and persecution or abandonment. However, some patients suffer a sense of not dreaming at all. Ms X was aware that she was dreaming and her dreams repeated her day time feelings and thoughts. However she was not always able to distinguish between her thoughts while she was trying to sleep and her sleeping dreams, as they ran into

each other and her sleep was so restless. Exposure to mercury seems to have a marked effect on the sleeping patterns and dreams of affected patients, and insomnia may be an important early symptom to recognise in mercury exposed patients, as it is commonly mentioned as one of the first symptoms presented.

Ms X's initial psychiatric symptoms were highly consistent with the literature. The psychiatric components most commonly associated with erythism, the syndrome caused by mercury toxicity, are nervousness and timidity, shyness, avoidance of people, irritability, noticeable mood changes, depression and anxiety (Cordeiro Júnior et al, 2003; Haut et al., 1999; Lishman, 1987, as cited in O'Carroll et al., 1995). Although paranoia is not often mentioned by name as a symptom in the literature, apprehensive thoughts of persecution, fear and nervousness are frequently referred to, and these suggest paranoid thought processes in mercury poisoned patients (Clarkson, et al., 2003; Cordeiro Júnior et al., 2003; O'Carroll et al., 1999; Powell, 2000, Rossini, et al., 2000, Uzzel, 1988). This is constant with Ms X's experience because her paranoid thoughts carry a theme of persecution and fear of attack. The content of her paranoia seems to be affected by cultural and situational variables, as much of her paranoia was contextually relevant.

Ms X did not report feeling shy or timid but was less sociable and became socially withdrawn for reasons of paranoia and irritability, which corresponds with the literature. She had to resign from her work with children because she became too irritable and aggressive. The literature describes mercury exposed patients to have increased irritability and aggression, even at low exposure levels (Echeverria et al., 2005; Ngim et al., 1992; Tang & Li, 2006, Uzzel, 1988). The literature is also aligned Ms X's psychotic symptoms, such as her auditory hallucinations and psychotic thought processes which resulted in her paranoid thoughts and reactions, such as running away from people she perceived as dangerous. The literature documents psychotic behaviour such as hallucinations and bizarre behaviours in mercury toxic patients and describes patients as suffering from psychosis (Powell, 2000, Uzzel, 1988).

Anxiety and depression are frequently referred to in the literature concerning mercury poisoning. In some cases, depression is one of the more persistent problems and is co-morbid with insomnia. However it is suggested that depression and anxiety in patients with mercury toxicity can be successfully treated with anti-depressants (Cordeiro Júnior et al., 2003; Haut et al., 1999). Ms X was not diagnosed with severe depression, however during her self-report she mentioned having self-defeating thoughts that minimised her self-worth, that she felt unreasonable guilt and conceded to us that she was depressed. Her depression may have been

in response to the trauma of mercury poisoning and life changes she was facing and not specifically a result of the mercury in itself. This corresponds with conclusions from other research that depression may be co-morbid with mercury poisoning as a reaction to the trauma of the illness, and not necessarily a direct cause of the mercury exposure (Bakir et al., 1980, Cordeiro Júnior, et al., 2003; Haut et al., 1999; Powell, 2000). Her anxiety was more marked and was coupled with her paranoia and general nervousness. Of all her symptoms, anxiety has been the most persistent, as she still currently considers herself more anxious and hypervigilant than she was before mercury exposure and still exhibits mild paranoia, as she will get a fright if she detects fast movements in others. It is interesting that Ms X is no longer suffering from insomnia, as in the literature, fatigue and insomnia are normally extremely persistent and permanent (Cordeiro Júnior, et al., 2003; Rossini, et al., 2000). It could be possible that her medication, which is a very mild tranquiliser, may be enabling her to sleep better. However it must also be considered that she was not exposed to high enough concentrations of mercury for a long enough period of time for it to inflict permanent damage to sleep regulation.

Although literature suggests that the limbic system is not as severely affected as the cerebral cortex, and is generally spared from structural damage, there have been suggestions that dysregulation of sub-cortical structures may induce psychiatric symptoms such as heightened anxiety (O'Carroll et al., 1995). This may be the case with Ms X; however, when analysing her results it is reasonable to conclude that she suffered greatest dysfunction in the frontal lobes and was thus unable to rationally contain her fears and emotions.

Unfortunately no functional scans, such as Positron Emission Tomography (PET), were done to measure the activity levels or functionality of Ms X's brain; therefore we can only speculate about which areas were most dysfunctional.

**Limitations and Future Directions**

A limitation to this study is that the patient was first assessed a month after she had stopped being exposed to mercury. This may have limited the findings from her first assessment, as much of the mercury had already left her system and she was on her way to recovery. This can be seen from her urine samples which dropped from 20. 71 µg / g creatinine on the 2nd February 2009 to 4.77µg / g creatinine 24th February 2009. Furthermore, her urine samples were taken after she was no longer being exposed to mercury, thus her mercury levels may have been much higher during the acute stages of mercury toxicity. The results from this research, especially the neurocognitive test results, would have been more accurate had the patient been assessed earlier and her urine samples been taken sooner.

However, the rationale for this research was that clinical descriptions for inorganic mercury toxicity are inadequate and do not provide medical practitioners with enough information to effectively assess and treat mercury exposed patients. Therefore, despite the time frame, the scarcity of mercury poisoning cases means that one needs to start by assessing whatever patients are available.

A second limitation is that the patient did not undergo any functional brain imaging. The literature suggests that MRI is ineffective for detecting structural brain damage as a result of mercury toxicity (Hunter & Russell, 1954; Nierenberg et al., 1998). Therefore, more useful results have been attained using SPECT scanning (O'Carroll et al., 1995). However, it is not confirmed that functional imaging is a more reliable method for analysing neurological effects of mercury in humans and more research is needed to confirm this. Nevertheless, the assessment of the patient was insufficient and slow to begin with due to a lack of knowledge about mercury toxicity, since greater knowledge may have lead to functional scanning being done as well as earlier detection of the disorder. In fact, had the patient not suspected mercury poisoning herself and suggested it to the medical practitioners, she may have not been assessed and diagnosed for a much longer period of time. Hopefully, in light of this research, future cases will be dealt with more effectively and swiftly.

## CONCLUSIONS

A case study of a single patient diagnosed with mercury toxicity was done over three separate neurocognitive assessment spanning almost two years, in order to identify the typical neuropsychological characteristics of mercury poisoning. Although the patient showed some slight long-term memory, working memory and attention deficits, it is reasonable to conclude that her cognitive defects are primarily due to dysfunction in the frontal lobes and an inability to integrate cognitive processes effectively, as opposed to being caused by limbic dysfunction. Furthermore, her psychiatric symptoms, such as paranoia, irritability, aggression, insomnia, auditory hallucinations, anxiety and social withdrawal, can be understood in terms of frontal lobe dysfunction as she could not control limbic functions in a rational manner.

Depression and anxiety may be perpetuated by the traumatic experience of mercury toxicity that the patient suffered, however it can be successfully treated with appropriate medication. In the case of this patient, the prescribed tranquillisers may be enabling her to sleep better as insomnia appears to be a permanent disability in mercury toxic patients and her expression of insomnia and dreaming were otherwise remarkably similar to those

reported in the literature.

Her procedural memory and learning deficits and particular motor defects, such as a resting tremor and ideational apraxia suggest that mercury exposure may also have caused lesions in the basal ganglia, but her dysmetria and poor co-ordination suggest cerebellar lesions. The patient showed evidence that damage of the cortex extended back laterally to the perisylvian areas as she showed cortical spatial difficulties despite having no perceptual problems.

Along with the clinical picture of the acute phase of mercury toxicity that the case of Ms X has provided, we can also draw a tentative conclusion that mercury toxicity follows a similar recovery path as traumatic brain injury. As such spontaneous recovery occurs over the first two years since the acute phase of mercury toxicity with the majority of recovery occurring over the first six months.

A final conclusion is that there is clearly a desperate need for more research on inorganic mercury toxicity and for this research to be filtered into the medical systems so that patients can be fairly assessed. It is not acceptable that patients be subjected to months of physical and emotional trauma because doctors do not have access to descriptions of typical clinical pictures associated with mercury toxicity. It is hoped that the findings from this research will help prevent this from occurring in the future.

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**Appendix 1**

**INFORMATION SHEET**

Dear Sir/Madam,

As you have already been assessed and diagnosed with mercury poisoning, we invite you to take part in a research study for the Department of Psychology, at the University of Cape Town, where we will assess effects of mercury toxicity on your cognitive functioning. Your participation is voluntary and will have no impact on your continued medical treatment.

**About the Research**

The reason we want to do this research is to develop a better description of how mercury poisoning affects the cognition of adults. At the moment, there is not a clear set of clinical characteristics that medical practitioners and psychologists can look for, when doing an assessment of mercury poisoning in their patients. The hope is to use the information from this research in combination with findings from other research to build a more complete picture of mercury poisoning. The conclusions from this research will be used to supplement another larger project, which is the compilation of a textbook that provides both medical doctors and psychologists with the clinical characteristics of numerous neuropsychological and neurological disorders. Mercury poisoning will be included in one of the chapters of this book.

There are practical ways in which this research will benefit society. For example, it is difficult for medical doctors and psychologists to conduct a clinical assessment without clear guidelines of what to look for and what to expect. People that have had exposure to mercury need correct assessment in order to receive the right treatment. Having a set of accurate clinical characteristics will assist medical practitioners to gauge mercury toxicity in their patients efficiently and correctly. Having a set of clinical characteristics may also enable practitioners to provide a more accurate prognosis to their patients. As mercury poisoning can have life-changing effects knowing what to expect may help those suffering from mercury toxicity to adapt and come to terms with related disabilities and lifestyle changes.

A second example of a practical outcome from this research is that clinical characteristics will enable investigations for litigation purposes to be more efficient. One of the more common places for inorganic mercury exposure is in industrial settings where mercury is used. Mercury toxicity can be so debilitating that sufferers of the condition can no

longer work. Employees and the families of employees who are now disabled because of exposure to mercury in their work place, through no fault of their own, should be able to claim for damages from the industry and to apply for disability grants. This may be particularly poignant in situations where industries have not educated their employees about the hazards of mercury and mercury vapour and have not invested in and enforced safety protocol and procedures. A set of clinical characteristics will protect both employees and employers from unjust litigation outcomes and may enable faster litigation procedures.

**Participant's Involvement**:

*What is involved:* The assessment will involve approximately three hours of your time. An experienced Neuropsychologist, Mark Solms, will assess you at the Groote Schuur Hospital. The assessment will include a detailed interview, cognitive tests, and a closing interview.

The interview will require information about your experience of changes in cognition since you were exposed to mercury, as well as physical and psychological changes. We will require information about your level of mercury toxicity and how you were exposed to mercury. Your medical history, sex, age, general health status, education level, occupation, social-economic status, and preferred language will also be required. We may require additional information about your health and lifestyle. You are not required to disclose any information that you may feel uncomfortable sharing. The interview will take approximately thirty minutes.

The type of cognitive tests to be used will be decided upon after the interview and during the assessment. However, all tests are typical, standard psychological tests that will require you to solve puzzles and complete various tasks and exercises, such as remembering numbers or a story. All of these tests are safe and are unlikely to cause any harm. The testing stage will take approximately two hours.

The final interview will be a discussion about the assessment and research where you may raise any questions or concerns you have not already brought up or have felt have not been adequately answered.

The assessment will be video recorded for our research purposes only. This is to enable us to ensure accurate interpretation and comparison of the results and to draw accurate

conclusions. Shandré Kerr a postgraduate in psychology will take written observations of the assessment. The results from the assessment will also be scribed by Solms.

All the information we take from the assessment will be kept confidential and will not be used for any other purpose without your written, informed consent. No identifying information will be used in the research or for any other purpose. All the data from the assessment will be stored in a password file or locked away, separate from any identifying information. We will assign you a random number in order to protect your confidentiality and will not record you name or address on anything except the consent form, which will be stored separately from all other research data.

The video recording will be destroyed after it has been transcribed to eliminate any identifying information. All computer-based records will be protected by passwords to which only Solms and Kerr will have access. All paper-based records and video recordings will be kept in a secure place where only Solms and Kerr have access to them. Solms and Kerr have signed an agreement to protect your confidentiality.

You may withdraw from the research program at any stage and are free to ask questions and raise concerns throughout the assessment. Your withdrawal from the research will have no impact on your continued medical treatment. You will not suffer any repercussions should you chose to withdraw.

When the research is written up, we will not mention any identifying information at any stage of any draft or final piece of work.

We will not be offering payment for you participation; however we will reimburse your travelling costs to the value of R100.00 only.

*Risk*s: There are no risks associated with this study. You may find tasks in the tests more challenging and this may cause you discomfort. However, if you feel uncomfortable at any time, for any reason, please feel free to mention it to Solms or Kerr so we can discuss your emotions with you. Solms will be able to provide you with psychological support during the assessment should you require it and will be able to refer you to suitable consulting professionals should you require. You may withdraw from the study without any negative consequences for yourself or the study. All data will be kept confidential and will only be used for research purposes.

*Benefits:* There are no direct benefits for participating in this study, except greater understanding about how mercury toxicity has affected your cognitive functioning. However, we will provide you with a written report of your assessment for your personal use.

There is no information that we want to withhold from you about the research or your involvement and rights as a participant in this study. Therefore, if you have any queries or concerns about this research, your involvement as a participant or your rights as a participant, please do not hesitate to ask.

We will ask you to sign a consent form before you may participate in the research.

You may email Shandré Kerr on shankerr2010@gmail.com with any queries or concerns or may ask any questions before or during the assessment should you decide to participate.

Thank you

Regards

Shandré Kerr

(Principal investigator and UCT Psychology Honours student)

**Appendix 2**

## INFORMED CONSENT FORM

**Title of Research Study**: The cognitive sequelae from Mercury exposure in human adults: Searching for characteristic features

**Name of Principal Researcher**: Shandré Jessica Kerr

**Department/Research Group Address**: Psychology Department

Faculty of Humanities

University of Cape Town

**Telephone**: 0723422224

**Email**: shankerr2010@gmail.com

**Name of Participant**: _____

As you have already been assessed and diagnosed with mercury poisoning, we invite you to take part in a research study for the Department of Psychology, at the University of Cape Town, where we will assess effects of mercury toxicity on your cognitive functioning. Your participation is completely voluntary and will have no impact on your continued medical treatment.

**Participant's Involvement**:

*What is involved:* The assessment will involve approximately three hours of your time. An experienced Neuropsychologist, Mark Solms, will assess you at the Groote Schuur Hospital. The assessment will include a detailed interview, cognitive tests, and a closing interview.

The interview will require information about your experience of changes in cognition since you were exposed to mercury, as well as physical and psychological changes. We will require information about your level of mercury toxicity and how you were exposed to mercury. Your medical history, sex, age, general health status, education level, occupation, social-economic status, and preferred language will also be required. We may require additional information about your health and lifestyle. You are not required to disclose any

information that you may feel uncomfortable sharing. The interview will take approximately thirty minutes.

The type of cognitive tests to be used will be decided upon after the interview and during the assessment. However, all tests are typical, standard psychological tests that will require you to solve puzzles and complete various tasks and exercises, such as remembering numbers or a story. All of these tests are safe and are unlikely to cause any harm. The testing stage will take approximately two hours.

The final interview will be a discussion about the assessment and research where you may raise any questions or concerns you have not already brought up or have felt have not been adequately answered.

The assessment will be video recorded for our research purposes only. This is to enable us to ensure accurate interpretation and comparison of the results and to draw accurate conclusions. Shandré Kerr a postgraduate in psychology will take written observations of the assessment. The results from the assessment will also be scribed by Solms.

All the information we take from the assessment will be kept confidential and will not be used for any other purpose without your written, informed consent. No identifying information will be used in the research or for any other purpose. All the data from the assessment will be stored in a password file or locked away, separate from any identifying information. We will assign you a random number in order to protect your confidentiality will not record your name or address on anything except the consent form, which will be stored separately from all other research data.

The video recording will be destroyed after it has been transcribed to eliminate any identifying information. All computer-based records will be protected by passwords that only Solms and Kerr will have access to. All paper-based records and video recordings will be kept in a secure place where only Solms and Kerr have access to them. Solms and Kerr have signed an agreement to protect your confidentiality.

You may withdraw from the research program at any stage and are free to ask questions and raise concerns throughout the assessment. Your withdrawal from the research will have no impact on your continued medical treatment. You will not suffer any repercussions should you chose to withdraw.

When the research is written up, we will not mention any identifying information at any stage of any draft or final piece of work.

We will not be offering payment for you participation; however, we will reimburse your travelling costs to the value of R100.00 only.

*Risk*s: There are no risks associated with this study. You may find tasks in the tests more challenging and this may cause you discomfort. However, if you feel uncomfortable at any time, for any reason, please feel free to mention it to Solms or Kerr so we can discuss your emotions with you. Solms will be able to provide you with psychological support during the assessment should you require it and will be able to refer you to suitable consulting professionals should you require. You may withdraw from the study without any negative consequences for yourself or the study. All data will be kept confidential and will only be used for research purposes.

*Benefits:* There are no direct benefits for participating in this study, except greater understanding about how mercury toxicity has affected your cognitive functioning. However, we will provide you with a written report of your assessment for your personal use.

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Please sign if you have

1) Read all the information and understand it, and
2) You agree to take part in the study.

**Signature of Participant**: _____

**Name of Participant**: _____

**Signature of Shandré Kerr, Principal Researcher**: _____

**Date**: _____

## Appendix 3

UNIVERSITY OF CAPE TOWN

**Health Sciences Faculty**
**Research Ethics Committee**
**Room E52-24 Groote Schuur Hospital Old Main Building**
**Observatory 7925**
**Telephone** [021] 406 6626 • **Facsimile** [021] 406 6411
**e-mail:** shuretta.thomas@uct.ac.za

**27 July 2010**

**HREC REF: 345/2010**

**Ms S Kerr**
**c/o Dr M Solms**
Psychology Department

Dear Ms Kerr

**PROJECT TITLE: THE COGNITIVE SEQUELAE FROM MERCURY EXPOSURE IN HUMAN ADULTS: SEARCHING FOR CHARACTERISTIC FEATURES.**

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee for review.

It is a pleasure to inform you that the Ethics Committee has **formally approved** the above-mentioned study.

**Approval is granted for one year till the 15th August 2011.**

Please submit an annual progress report if the research continues beyond the approval period. Please submit a brief summary of findings if you complete the study within the approval period so that we can close our file.

Recommendations:

1. Please consider simplifying some of the terms in the information sheet and consent form such as toxicity (poisoning), cognitive, observations (notes) as these may be unfamiliar to participants.
2. Please add the contact details for the Human Research Ethics Committee should participants have any queries regarding their Rights as research subjects.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

**Please quote the REC. REF in all your correspondence.**

**S Thomas**

## ETHICAL CONSIDERATIONS

The proposed research is designed so as not to harm or wrong patients in any way at any stage of their inclusion in the research. We made specific ethical considerations to ensure this. We have ethics approval from the University of Cape Town Department of Psychology Research Ethics Committee. Because we are using a clinical sample, we also have ethics approval from the University of Cape Town Faculty of Health Sciences Research Ethics Committee. The proposed research adheres to the Helsinki Declaration of 2008 and complies with UCT's intellectual property rights policy. As neither Kerr nor Solms are registered with the Health Professions Council of South Africa, Dr Ozayr Ameen will be a co-investigator for the proposed research (Registration number: MP04344981.)

## AUTHOR'S NOTE

### Acknowledgements

I would like to acknowledge the following for their assistance with this research:

My Supervisor, Prof. Mark Solms for his guidance and shared knowledge

Elena For organising so much and being the support behind the all the activity!

Ross Balkin for all his time and assistance and invaluable guidance.

Dr Dave Knight for sharing his information about the case.

Chris du Plooy for sharing his extremely useful information about the case, with which this study would not be possible.

The staff at Groote Schuur Hospital for their time and effort.

Ms X, for being so kind as to share her experience of mercury toxicity