The Middelheim Frontality Score: a behavioural assessment scale that discriminates frontotemporal dementia from Alzheimer’s disease

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SUMMARY

Background Despite striking neuropsychological and behavioural differences between Alzheimer’s disease (AD) and frontotemporal dementia (FTD), clinical diagnostic criteria failed to discriminate FTD from AD patients. We therefore developed the Middelheim Frontality Score (MFS), a disease-long clinical and behavioural assessment tool that measures frontal lobe features, and set up this prospective study in clinically diagnosed AD and FTD patients to assess discriminatory power and intra- and inter-rater variability.

Methods Patients with probable AD (n = 400) and FTD (n = 62) were included. The MFS was obtained by summatig the scores obtained in a standardized fashion on ten items yielding a total maximal score of 10. Information was obtained through an interview of the patient and her/his caregiver, clinical files and behavioural observation.

Results Comparing mean total MFS scores, FTD patients (6.3 ± 1.8) had significantly higher scores than AD patients (3.1 ± 1.8) (p < 0.001). Distribution of scores on individual MFS items was significantly different between both disease groups (χ² = 76.2; p < 0.001). A moderately positive and highly significant correlation was shown between the total MFS score and diagnosis FTD (r = 0.478; p < 0.0001). Applying a total MFS score of 5 as discriminatory cut-off, a specificity of 89.0% and a sensitivity of 88.7% were achieved. Intra- and inter-rater variability was calculated in a different study population by means of retest correlation, revealing moderate to strong positive correlations of high statistical significance.

Conclusions The MFS is a clinical and behavioural assessment scale that measures frontal lobe features and that was shown to reliably discriminate FTD from AD patients. Copyright © 2004 John Wiley & Sons, Ltd.

KEY WORDS — dementia; behaviour; Alzheimer’s disease; frontotemporal lobar degeneration; frontotemporal dementia

INTRODUCTION

With the development of new treatments for Alzheimer’s disease (AD) that may not to be efficacious in the treatment of frontotemporal dementia (FTD), there is an increasing need for distinguishing FTD from AD. Moreover, a different prognostic profile of AD versus FTD strengthens the need for (early) differential diagnosis. Despite striking neuropsychological and behavioural differences between AD and FTD, NINCDS-ADRDA criteria failed to differentiate AD from FTD as many FTD patients fulfil the NINCDS-ADRDA criteria of AD (Varma et al., 1999). Although a combination of behavioural, neuropsychological and physical findings was useful in distinguishing FTD from AD (Rosen et al., 2002), behavioural quantification appeared to be more sensitive than cognitive testing in FTD (Kertesz et al.,

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2003). Our Memory Team therefore developed the Middelheim Frontality Score (MFS) as a measure for frontal lobe features. Based on observational studies (Gustafson, 1987; The Lund and Manchester Groups, 1994; Neary et al., 1998), we selected ten items for inclusion in the MFS. In order to assess discriminatory power and reliability of the MFS, we set up a prospective study in clinically diagnosed AD and FTD patients. Given the foreseen heterogeneity and unequal numbers of patient groups due to consecutive inclusion of eligible patients, validity was as well tested in subgroups of: (1) neuropathologically confirmed AD and FTD patients; (2) mildly demented AD and FTD patients and (3) for gender and severity matched AD and FTD pairs.

MATERIAL AND METHODS

Study population

Both in- and out-patients with dementia of all stages were consecutively recruited from our Memory Clinic for inclusion in this prospective study. The study population consisted of patients with probable AD (n = 400) and patients with FTD (n = 62). All patients underwent a general physical and neurological examination, routine blood screening, neuroimaging consisting of brain computerized tomography scan and/or magnetic resonance imaging, standard electroencephalogram and an extensive neuropsychological examination with emphasis on frontal lobe tests. Clinical diagnosis was made by consensus by at least two neurologists (SE, JG, BAP, PPDD) who were blinded to MFS scores. Mini-Mental State Examination (MMSE) scores were obtained according to Folstein et al. (1975).

Diagnosis of probable AD was based on NINCDS/ADRDA criteria (McKhann et al., 1984) though all patients fulfilled the Diagnostic and Statistical Manual of Mental Diseases (DSM-IV) (American Psychiatric Association, 1994) criteria as well.

Diagnosis of FTD was based on clinical diagnostic criteria for FTD (Neary et al., 1998). All FTD patients fulfilled the core diagnostic features and several supportive diagnostic features. History of the syndrome was considered along with extensive neuropsychological assessments revealing a characteristic neurocognitive profile of disproportionate executive dysfunction indicating frontal lobe involvement and objectifying the insidious onset and the progressive course of the disease. In accordance with the diagnostic criteria of FTD (Neary et al., 1998), functional brain imaging (single photon emission computed tomography, SPECT) was used to support the clinical diagnosis of FTD as we described earlier (Pickut et al., 1997).

Inter- and intra-rater variability was tested in a different study population that was also recruited from our Memory Clinic and that consisted of patients (n = 56) with several forms of dementia: AD (n = 30), FTD (n = 1), mixed dementia (n = 13), vascular dementia (n = 5), dementia with Lewy bodies (n = 2), Parkinson’s disease dementia (n = 3), progressive supranuclear palsy (n = 1) and normal pressure hydrocephaly (n = 1).

Resulting from longitudinal follow-up, 20 included AD and three FTD patients have been autopsied so far, allowing neuropathological confirmation of the clinical diagnosis in this subpopulation. For AD patients, the neuropathological criteria of Braak and Braak (1991) and Jellinger (1998) were applied whereas FTD patients were neuropathologically diagnosed according to Jackson and Lowe (1996) and Markesbery (1998).

All patients and caregivers gave informed consent for participation to the study that was approved by the local ethics committee.

MFS

The MFS was rated by a clinician and was obtained by summatng the scores obtained in a standardized fashion on ten items. Each item was scored either zero (absent) or one (present) yielding a total maximal score of 10. All items that the patient had displayed since disease onset were scored one. Information was obtained through an interview of the patient and her/his professional and/or main caregiver, clinical files and behavioural observation. The rater used a form listing all items to be addressed. For the interview, a series of prespecified questions were asked. For details please see Appendix 1.

The ten items scored were: (item 1) initially comparatively spared memory and spatial abilities that reflects the neurobehavioural onset of the disease; frequently occurring personality and behavioural changes like: (item 2) loss of insight and judgement, (item 3) disinhibition, (item 4) dietary hyperactivity (referring to overeating), (item 5) changes in sexual behaviour (hypersexuality as well as the more frequently occurring hyposexuality), (item 6) stereotyped behaviour (encompasses all kinds of stereotyped behaviour, both simple repetitive behaviours (can also be oral) as complex behavioural routines as wandering), (item 7) impaired control of emotions, euphoria or emotional bluntness, (item 8) aspontaneity; (item 9) speech disturbances such as stereotyped phrases, logorrhoea, echolalia, mutism and finally, (item 10) restlessness.
All raters were (behavioural) neurologists, neuropsychiatrists or neuropsychologists, experienced in dementia and were blinded to each other’s ratings in case of inter-rater variability. To determine intra- and inter-rater reliability, a population of 56 inpatients was assessed two times within a timeframe of one week by four raters who were blinded to clinical diagnoses. Ratings were based on an interview of the main professional caregiver who provided information from behavioural observation, clinical files, an interview of the patient and of the non-professional main caregiver. For a detailed description of the instructions: see Appendix 1.

Statistical analyses

A student’s t-test or –when lacking normal distribution– a Mann–Whitney Rank Sum Test (RST) was used for comparison of the clinical and demographic data. Distribution of scores on individual MFS items was compared using Chi-square statistics. To test whether a high total score on the MFS and individual MFS item scores correlated with the diagnosis of FTD, a Spearman Rank-Order Correlation was calculated. Based on MFS total scores, a predictive model of diagnostic group membership was built using discriminant analysis. Inter-rater reliability and intra-rater reliability were tested by means of a Spearman Rank-Order Correlation.

The same analyses were performed in subsets of patients with mild dementia (MMSE total score >22), patients with neuropathologically confirmed diagnoses and pairs of AD and FTD patients, matched for gender and MMSE score or Behave-AD global scores.

A probability level of \( p < 0.05 \) was considered significant. Analyses were performed using SigmaStat software (SPSS Science, Erkrath, Germany) and SPSS for windows 10.0 (discriminant analysis).

RESULTS

Demographic, clinical and neuropathological data

Demographic and clinical data of AD and FTD patients are summarised in Table 1. AD patients were significantly older and more severely cognitively deteriorated at inclusion than FTD patients. Distribution of male/female ratios was significantly different among the patient groups: the AD group contained more females than men, whereas the male/female ratio was inverted in the FTD population.

The clinical diagnosis was confirmed neuropathologically in the 20 probable AD patients who came to autopsy. Three clinically diagnosed FTD patients were neuropathologically diagnosed as Pick’s disease \((n = 1)\), frontal dementia lacking distinctive pathology \((n = 1)\) and FTD with motor neuron disease \((n = 1)\).

MFS

Comparing mean total MFS scores of FTD patients with those of AD patients, a high level of statistical significance was achieved with FTD patients having higher scores than AD patients (Table 1). Distribution of scores on individual MFS items was significantly different comparing both disease groups (Table 2) \((\chi^2 = 76.2; p < 0.001)\). Besides item 2 (loss of insight and judgement), all MFS items correlated significantly with the diagnosis of FTD, revealing the strongest correlation for item 1 (initially comparatively spared memory and spatial abilities) (Table 2). A moderately positive and highly significant correlation was shown between the total MFS score and diagnosis FTD (Table 2). Sensitivities and specificities of different total MFS scores for discriminating FTD from AD are displayed in Table 3. Applying a total MFS score of 5 as cut-off, a specificity of 89.0% and a sensitivity of 88.7% was achieved. Figure 1 displays the ROC graph for the MFS discriminating FTD from AD patients. At a total MFS score of 5, the positive predictive value (PPV) and negative predictive value for a diagnosis of FTD was 0.37 and 0.98 respectively. PPV gradually increased to 1.00 at a total MFS score of 9 (MFS total score of 6: PPV = 0.51; MFS total score of 7: PPV = 0.70; MFS total score of 8: PPV = 0.77; MFS total score of 9: PPV = 1.00).

By means of a predictive model of diagnostic group membership that was built using discriminant analysis based on MFS total scores, 78.6% of patients were correctly classified in their diagnostic categories.
Considering all MFS item scores, 88.8% of patients were correctly classified.

Intra- and inter-rater variability

Intra- and inter-rater variability was calculated by means of retest correlation. Moderate positive intra-rater correlations (rater 1: \( R = 0.757 \); rater 2: \( R = 0.741 \); rater 3: \( R = 0.728 \); rater 4: \( R = 0.654 \)) of high statistical significance (\( p < 0.0001 \)) were found. Inter-rater variability calculation revealed strong (rater 1–2: \( R = 0.990 \); rater 1–3: \( R = 0.971 \); rater 1–4: \( R = 0.970 \); rater 2–3: \( R = 0.959 \); rater 2–4: \( R = 0.939 \); rater 3–4: \( R = 0.932 \)) and highly significant (\( p < 0.0001 \)) correlations.

MFS in subgroups of neuropathologically confirmed AD and FTD patients

Comparing mean total MFS scores of definite FTD (9.0 ± 1.0) with definite AD (3.1 ± 2.1) patients, a high level of statistical significance was achieved.
MFS in subgroups of mildly demented AD and FTD patients

Based on MMSE scores > 22, subgroups of mildly demented AD (n = 42) and FTD (n = 24) patients were selected. The mean total MFS score was significantly higher in FTD (5.7 ± 2.5) than in AD patients (2.5 ± 1.7) (p < 0.001). The total MFS score correlated with the diagnosis of FTD, reaching levels of high statistical significance (R = 0.665; p < 0.0001). Based on MFS total scores, 83.3% of patients were correctly classified in their diagnostic groups applying discriminant analysis. Considering all MFS item scores, 87.9% of patients were correctly classified. Sensitivity and specificity were calculated in subgroups of mildly demented AD and FTD patients (MMSE scores > 22) revealing a sensitivity and specificity of 91.7% and 85.7% for a total MFS score of 4 and a sensitivity and specificity of 79.2% and 92.9% for a total MFS score of 5.

MFS in subgroups of AD and FTD patients, matched for Behave-AD global scores

Based on 29 FTD patients for whom Behave-AD scores were available, 29 AD patients were selected, matched for Behave-AD global scores. The two subgroups did not differ with regard to male/female ratios (p = 0.428) and MMSE scores (p = 0.308). The mean total MFS score was significantly higher in FTD (6.6 ± 1.3) than in AD patients (3.2 ± 1.7) (p < 0.001). Based on MFS total scores, 86.2% of patients were correctly classified in their diagnostic groups applying discriminant analysis. Considering all MFS item scores, 91.4% of patients were correctly classified. A strong and highly significant correlation between the total MFS score and diagnosis FTD was revealed (R = 0.755; p < 0.0001).

DISCUSSION

Although the Neuropsychiatric Inventory was able to correctly classify 77% of AD and FTD patients (Levy et al., 1996), frequently used behavioural assessment scales like the Behavioural Pathology in Alzheimer’s Disease Rating Scale (Behave-AD) and the Cohen-Mansfield Agitation Inventory lack sensitivity for FTD as they have specifically been developed for AD. The Behave-AD even underestimate behavioural and psychological signs and symptoms of dementia in FTD patients, as we recently demonstrated: FTD patients (n = 28) had significantly lower Behave-AD total scores (6.9 ± 4.7) than AD patients (n = 152) (11.0 ± 7.4; RST: p = 0.006) whereas the Behave-AD global scores (reflecting caregiver burden) were not different between both patient groups (FTD: 3.0 ± 1.9) than male AD patients (3.4 ± 1.7) (p = 0.017). In FTD patients, no significant differences in MFS total scores between male and female subjects were found (p = 0.718). Given the possible influence of gender and severity of dementia on the validity data of the MFS, we performed additional analyses in subgroups of 56 AD and FTD patients that were matched for gender and MMSE scores. The mean total MFS score was significantly higher in FTD (6.3 ± 1.6) than in AD patients (2.1 ± 1.6) (p < 0.001). Based on MFS total scores, 88.4% of patients were correctly classified in their diagnostic groups applying discriminant analysis. Considering all MFS item scores, 92.8% of patients were correctly classified. A strong and highly significant correlation between the total MFS score and diagnosis FTD was revealed (r = -0.798; p < 0.0001).
1.4 ± 0.8; AD: 1.6 ± 0.8; RST; p = 0.311) (Engelborghs et al., 2004). The present study demonstrates that FTD and AD can be discriminated by a behavioural assessment scale that measures frontal lobe features. Moreover, we have previously shown that the total MFS score correlates with severity of bifrontal hypoperfusion on SPECT in FTD (Pickut et al., 1997).

The validation of the MFS was mainly performed in clinically diagnosed AD and FTD patients, which may be considered a drawback of the present study since several MFS items form part of the clinical diagnostic criteria of FTD, like emotional blunting, loss of insight, stereotyped behaviour, aspontaneity, echolalia and mutism (Neary et al., 1998). Although we cannot rule out that the FTD group did not contain AD patients and vice versa, the demographic and clinical differences between both patient groups are in accordance with formerly published studies, indicating that the FTD population included is a representative sample (Ratnavalli et al., 2002). Moreover, preliminary validity testing in a limited sample of 23 neuropathologically confirmed FTD and AD cases, revealed a discriminatory power that was comparable to the discriminatory power in clinically diagnosed patients. In order to allow testing of validity in an extended population of neuropathologically confirmed cases, follow-up of the included patients is ongoing.

In order to rule out a possible bias by gender and dementia severity, we retested validity in a subgroup consisting of 56 AD and FTD pairs, matched for gender and MMSE scores. The discriminatory power of the MFS was comparable to the data we obtained in the total population. Meanwhile, this analysis ruled out a limited accuracy of comparison due to the unequal numbers of patients in both patient groups. As the differential diagnosis AD-FTD is most challenging in the earliest stages of the disease, we repeated validity testing of the MFS in a subset of mildly demented patients, which resulted in good discriminatory power. Moreover, discriminant analysis applying all MFS items showed that 88% of mildly demented AD and FTD patients were correctly classified in their diagnostic groups. As the MMSE mainly relies on memory and orientation but does not contain any items on executive functions, MMSE scores might underscore dementia severity in FTD patients. Therefore, matching both disease groups by Behave-AD global scores that reflect caregiver burden might be a better way to equate both disease groups. This strategy to constitute the comparison between both diagnostic groups again demonstrated a good discriminatory power for the MFS.

In accordance with the generally accepted criteria for diagnostic biological markers for AD (The Ronald and Nancy Reagan Research Institute of the Alzheimer’s Association and the National Institute on Aging Working Group, 1998), one could assume that a sensitivity and specificity of at least 80% should be achieved for a cut-off score to reliably allow discriminating FTD from AD. Given the favourable values of both sensitivity and specificity, a total MFS score of 5 was chosen as discriminatory cut-off. Applying this cut-off score, respectively 85.9% and 76.6% of clinically diagnosed FTD and AD patients were correctly classified. At a cut-off score of 5, the PPV was low (0.37), increasing to a value of 1.0 at a MSF total score of 9. As the MFS score correlated negatively with the MMSE score in AD patients (R = −0.285; p < 0.0001), low PPV values might be explained by the fact that AD patients had rather advanced dementia at inclusion as reflected by a mean MMSE score of 14. It therefore can be assumed that PPV values will be higher if the MFS is applied in early dementia, when discriminating FTD from AD is often difficult.

The here presented data on validity of the MFS are better than those of validated assessment scales or diagnostic criteria as most do not achieve the 80% levels for both sensitivity and specificity. Among a group of AD and FTD patients, the worldwide used NINCDS-ADRDA criteria had a sensitivity of 93% and a specificity of only 23% (Varma et al., 1999). Applying a cut-off score of 24, the Mini Mental State Examination achieved a sensitivity of 52% and a specificity of 96% in discriminating demented subjects from normal controls (Mathuranath et al., 2000). Although the Hachinski Ischemic Score has not fully been validated, Gold et al. (1997) revealed a sensitivity of 43% and a specificity of 88% for discriminating VaD from AD patients.

Several test batteries that assess frontal lobe functions have already been developed. Some relied on neuropsychological and executive function deficits, whereas others combined behavioural and neuropsychological features. Using a discriminant model derived from the MMSE and the Executive Interview (EXIT), a bedside measure of executive function, Royall et al. (1994) were able to discriminate AD from FTD patients with a sensitivity and specificity of 83 and 85% respectively. Using component scores from the Addenbrooke’s Cognitive Examination, Mathuranath et al. (2000) developed the VLOM ratio (verbal fluency + language]/orientation + memory). Although the authors defined two different cut-off scores in order to optimise sensitivity and specificity for discriminating AD from non-AD and FTD from non-FTD
dementias, sensitivities remained below the 80% threshold with values of 75% and 58% respectively.

The Frontal Assessment Battery (FAB) is a short bedside cognitive and behavioural battery that accurately discriminated patients with frontal lobe dysfunction from normal controls (Dubois et al., 2000). Recently, the sensitivity and specificity of the FAB to differentiate FTD (n = 26) from AD (n = 64) was evaluated, correctly identifying 78.9% of patients (Slachevsky et al., 2004). In subgroups of mildly demented AD (n = 24) and FTD (n = 9) patients, the FAB differentiated FTD from AD patients with a sensitivity and specificity of 77 and 87% respectively (Slachevsky et al., 2004). The Frontal Behavioural Inventory (FBI) is a caregiver assessment scale that was specifically indicated to discriminate FTD from AD patients with a sen-
caregiver assessment scale that was specifically indicated.

tically confirmed cases with AD and FTD is

discriminates FTD from AD patients. Further classical behavioural assessment scales, reliably measures frontal lobe features that, in contrast to is a clinical and behavioural assessment tool that AD/FTD.

in discriminating patients with more advanced is based on both clinical observation and inter-

scale for all stages of AD and FTD. Indeed, back of the FBI is that it is entirely caregiver-

behaviour at the moment of the interview and as patients were included at the time of first diagnostic assessment, it can not be ruled out that the discriminatory power of the FBI decreases with disease progression. Indeed, disease progression may introduce new behaviours (e.g. apathy in AD patients) and may also lead to the disappearance of other symptoms (e.g. disinhibition in FTD patients). However, a longitudinal study on the FBI in 52 FTD and 52 AD patients, demonstrated the usefulness of behavioural quantification that appeared to be more sensitive than cognitive testing in frontotemporal dementia (Kertesz et al., 2003). A possible drawback of the FBI is that it is entirely caregiver-based which possibly limits its reliability in certain circumstances. In this study, we have shown that the MFS is a reliable discriminatory assessment scale for all stages of AD and FTD. Indeed, the MFS is a disease-long assessment scale and is based on both clinical observation and interview of caregivers, which are major advantages in discriminating patients with more advanced AD/FTD.

In conclusion, the Middelheim Frontality Score is a clinical and behavioural assessment tool that measures frontal lobe features that, in contrast to classical behavioural assessment scales, reliably discriminates FTD from AD patients. Further validation of this scale in a population of neuropathologically confirmed cases with AD and FTD is indicated.

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REFERENCES


Kertesz A, Davidson W, McCabe P, Munoz D. 2003. Behavioral quantitation is more sensitive than cognitive testing in frontotem-


The Lund and Manchester Groups. 1994. Clinical and neuropatho-


Varma AR, Snowden JS, Lloyd JJ, Talbot PR, Mann DMA, Royall DR, Mahurin RK, Cornell J. 1994. Bedside assessment of behavioural symptoms and memory decline, nine additional items evaluate behavioural areas. The MFS consists of ten items to be scored. While the first item relates to the temporal relationship between memory decline and spatial abilities and behavioural disturbances, the 9 following items attempt to evaluate behavioural alterations that may be manifestations of your [husband’s/wife’s/Mr Johnson’s/etc.] condition. In what follows, we describe the ten items in more detail and summarize the items that should be looked for in the different (behavioural) domains. For each item, we include one or some questions to be addressed to the informant. In addition, we add some further specifications for the rater in order to adequately score based on the interview, study of the clinical files and observations.

1. Initially comparatively spared memory and spatial abilities

**Question:** What was the first abnormality you observed? Alterations in your [husband’s/wife’s/Mr Johnson’s/etc.] behaviour or decline in memory or spatial abilities?
The rater scores based on information obtained from the carer, the clinical files and/or previous neuropsychological observations.

2. Loss of insight and judgement

**Question:** Does your [husband’s/wife’s/Mr Johnson’s /etc.] have impaired insight and/or judgmental problems? Have there been events (quite early in the disease) indicative of poor judgment with regard to practical e.g. financial or social issues?

Poor insight and judgment may manifest among others as buying unnecessary goods; poor financial judgment such as donating property and making wrong investments; making wrong and or impulsive decisions such as reckless driving, hit and run; leaving a baby or infant unattended; and stealing in stores or petty theft.

This item does not score for loss of insight in illness or lack of awareness of disease related disabilities. Judgment is defined as the capacity to anticipate consequences and to guide one’s behaviour in a culturally acceptable manner. Involved processes may be: reasoning, abstraction, planning and problem solving.

3. Disinhibition

**Question:** Has your [husband/wife/Mr Johnson/etc.] been acting impulsively (without thinking) or has your [husband/wife/Mr Johnson/etc.] been making socially inappropriate or tactless remarks. Does he/she do or say things that are normally not done or said in public? Did his/her behaviour cause embarrassment to you or others?

The types of behaviour scored here may also refer to inappropriate contact with strangers, inappropriate joviality, insensitive or hurting statements, sexual remarks, violation of interpersonal space, inappropriate physical contacts such as hugging and caressing and inappropriate sharing of personal and private matters.

4. Dietary hyperactivity

**Question:** Did the drinking or eating behaviour of your [husband/wife/Mr Johnson/etc.] change during the course of the illness? Does he/she put too much food in his/her mouth at once? Does he/she eat more or more frequently than before? Is he/she frequently searching for food? Does he/she eat faster than before and/or improperly? Do you need to limit his/her food intake? Are there any changes in food preferences (e.g. sweet foods)?

This item refers especially to the frequency, amount and/or way of eating. This may also include eating of foreign objects, choking from eating improperly, taking other’s food. Please note that changes in appetite (and accompanying weight gain or loss), which may be rather indicative of dysphoria, should not be scored here.

5. Changes in sexual behaviour

**Question:** Has there been a change in the nature or frequency (increase or decrease) of the sexual activities of your [husband/wife/Mr Johnson/etc.]? Has there been inappropriate sexual behaviour? Did your [husband/wife/Mr Johnson/etc.] make inappropriate verbal or physical sexual advances? Did the patient engage in unwanted fondling, caressing or kissing? Did your [husband/wife/Mr Johnson/etc.] display exhibitionistic behaviour, or masturbated publicly etc.?

Inappropriate disrobing without sexual intent should not be considered as a change in sexual behaviour.

6. Stereotyped behaviour

**Question:** Has your [husband/wife/Mr Johnson/etc.] developed stereotyped behaviour? Does the patient have repetitive activities or ‘habits’ that he/she performs over and over?

This may manifest as stereotypic movements, such as patting, tapping, rocking self, fiddling with something, twiddling with something, rubbing self or object, hand rubbing, hand clapping, sucking fingers, taking shoes on and off, picking at self, clothing, or objects, manipulation of nearby objects in a repetitious manner. Stereotyped behaviour may also consist of counting aloud, tune humming, dancing. Stereotyped behaviour may also manifest as frowning or grimacing, touching, pursing lips, chewing, grinding teeth, moving extremities, or more complex activities such as wandering a fixed route, collecting and hoarding objects, and rituals involving toileting and dressing.

7. Impaired control of emotions, euphoria or emotional bluntness

**Question:** Did the patient display impaired emotions when confronted with pleasant or sad events or situations? This behaviour may include apparent indifference or excessive emotional reactions such as excessive inappropriate laughing or crying. Does the patient find humour and laugh at things that others do not consider funny? Does the patient seem too
cheerful or too happy without reason? Is the patient’s regulation of emotional control impaired (e.g. rapid switching between sadness and happiness)? Is the patient uncaring about the emotional states of others around him/her?

Emotional bluntness includes loss of the capacity to demonstrate primary emotions (e.g. happiness, sadness, fear) and social emotions (e.g. embarrassment, sympathy and empathy).

8. Aspontaneity

**Question:** Has the patient been less involved in activities? Did he/she lose interest in his/her environment? Have there been examples of social withdrawal? Is he/she less engaged in conversation? Has the patient lost interest in friends and family members? Is the patient less involved in doing chores? Is the patient apathetic? Overall, does the patient seem less spontaneous and less active than usual? Did the patient loose his/her usual interests?

9. Speech disturbances such as stereotyped phrases, logorrhoea, mutism, echolalia

**Question:** Does your [husband/wife/Mr Johnson/etc.] have speech disturbances? These may include the utterance of stereotyped (repetitive) words, phrases, or entire themes or verbal automatisms. Has your [husband/wife/Mr Johnson/etc.] been constantly talkative or just the opposite? Does or did your [husband/wife/Mr Johnson/etc.] involuntarily, automatically repeat words or phrases said to him or others?

10. Restlessness

**Question:** Is your [husband/wife/Mr Johnson/etc.] more restless than before the onset of disease? This includes among others aimless wandering, pacing, fidgeting, always moving around in seat, getting up and sitting down, inability to sit still.

A total MFS score can be calculated by adding the scores of the ten items.

MFS SCORE SHEET

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<tr>
<th>Item to be scored</th>
<th>Present</th>
<th>Absent</th>
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<th>Score</th>
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<td>1 Initially comparatively spared memory and spatial abilities</td>
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<td>2 Loss of insight and judgement</td>
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<td>4 Dietary hyperactivity (referring to overeating)</td>
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<td>5 Changes in sexual behaviour</td>
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<td>7 Impaired control of emotions, euphoria or emotional bluntness</td>
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<td>8 Aspontaneity</td>
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<td>9 Speech disturbances such as stereotyped phrases, logorrhoea, echolalia, mutism</td>
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<td>10 Restlessness</td>
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<td><strong>Total Score</strong></td>
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