Brief Methodological Report

First Spanish Version of the Memorial Delirium Assessment Scale: Psychometric Properties, Responsiveness, and Factor Loadings

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Abstract

Context. The Memorial Delirium Assessment Scale (MDAS) is a reliable and validated instrument with which to assess delirium. However, MDAS responsiveness has only been investigated in an indirect way. Also, neurobehavioral and global cognitive factors seem to be the MDAS main factor loads.

Objectives. The primary objective of this study was to evaluate MDAS responsiveness and analyze individual factors on this scale. The secondary objective was to confirm concurrent validity and reliability of the Spanish version of the MDAS.

Methods. The translation-back translation method was used to obtain the Spanish version of the MDAS. Delirium diagnosis was determined by the clinical *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, Text Revision criteria and with the Confusion Assessment Method. Responsiveness and factor loadings were determined with the Delirium Rating Scale-Revised-98, the Mini-Mental State Examination (MMSE), and the MDAS at baseline (0 hours) and at 72 hours.

Results. Variation in the scores of the Delirium Rating Scale-Revised-98 shows a correlation of $r = 0.93$, with variation in MDAS scores at $P < 0.001$. Variation in MMSE scores shows a correlation of $r = -0.84$, with variation in MDAS scores at $P = 0.015$. Factor I, neurobehavioral (reduced awareness, reduced attention, perceptual disturbance, delusions, altered psychomotor activity, and sleep-wake cycle disturbance), correlated moderately with the MMSE at −0.56. Factor II, global cognitive (disorientation, short-term memory impairment, impaired digit

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span, and disorganized thinking), correlated strongly with the MMSE at −0.81. Factor II was significantly more reliable than Factor I, rho = 0.7, $P = 0.01$.

Conclusion. The high responsiveness confirms the value of the MDAS for ongoing delirium assessment. Two differentiated factor loadings point to a potential future need for MDAS subscales. J Pain Symptom Manage 2014;47:189−197.

Key Words
Delirium, assessment, monitoring, questionnaires, cancer

Introduction

Among patients with cancer, 50% will develop delirium; delirium incidence increases to 66% in patients with advanced cancer and to 80% in cancer patients at the end of life.[1−4] Delirium is a harbinger of serious illness and has been identified as a predictor of in-hospital mortality.[5] Delirium greatly contributes to patient and caregiver suffering[6] and is one of the first symptoms that may lead to palliative sedation.[7]

An effective delirium assessment allows for early diagnosis and better treatment.[1] Wong et al.[8] demonstrated that the diagnostic capacity of the Memorial Delirium Assessment Scale (MDAS) showed a likelihood ratio higher than 6 vs. an assessment by a health professional. The MDAS was developed by Breitbart et al.[9] in 1997 in accordance with the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, Text Revision (*DSM-IV-TR*) criteria. This scale has demonstrated good reliability, concurrent validity, and clinical application and has retained its psychometric characteristics in different languages.[9−12] However, MDAS responsiveness (the instrument's ability to detect patient changes) has been addressed in an indirect way, and factor analysis has only been investigated once, without strong consistency.

The reporting of MDAS responsiveness is necessary to confirm this tool's ability to assess delirium severity variations over time. MDAS factor loadings were defined by Lawlor et al.[10] as two primary correlated factors: neurobehavioral and global cognitive. They used loadings of 0.35 or higher for interpretation purposes and four MDAS items (impaired digit span, reduced awareness, altered psychomotor activity, and sleep-wake cycle disturbance) loaded onto both factors. We hypothesized that the MDAS demonstrates good responsiveness with its global cognitive and neurobehavioral loading factors. Thus, the main objective of this study was to evaluate MDAS responsiveness and analyze individual factors on the questionnaire. The secondary objective was to confirm concurrent validity and reliability of the Spanish version of the MDAS.

Methods

Between June 2011 and May 2012, 85 cancer patients with delirium residing in three palliative care units in Spain were evaluated: 37 patients at Hospital Centro de Cuidados Laguna Hospice, Madrid; 28 patients at Clínica Universitaria, Universidad de Navarra, Pamplona; and 20 patients at Hospital Universitario La Paz, Madrid. Delirium was diagnosed by a palliative care specialist according to *DSM-IV-TR* criteria and Confusion Assessment Method (CAM) findings. The institutional review boards at all three centers approved the study, and participants provided written informed consent. When that was not possible, the patient's caregiver provided consent.

We used translation and back translation methods to obtain a Spanish version of the MDAS, which was reviewed by experts.[13,14] Three palliative care professionals assessed three translations done by bilingual translators. Each translation was reviewed by a group of experts that evaluated clarity and common language on a 0-to-10 scale for each MDAS item. A definitive MDAS translation was developed using the three translations. The translation obtained was back translated to English, and the final version was sent to Dr. Breitbart; any comprehension difficulties were resolved,

and the final version was approved by Dr. Breitbart.

Participants

Inpatients were enrolled in the study if they met the following eligibility criteria: delirium diagnosis; age 18 years or older; diagnosis of advanced cancer; Palliative Performance Scale (PPS) score of 30 or higher; and informed consent signed by the patient or surrogate. Sociodemographic variables including patient age, gender, diagnosis, and cause of delirium were collected.

Instruments

PPS. The PPS[15] measures performance status based on ambulation capacity, level of activity, self-care, intake, and consciousness level of the patient. Scores range from 100%, indicating good health, to 0%, indicating death.

CAM. This instrument is a diagnosis algorithm for identification of delirium and assesses the presence, severity, and fluctuation of delirium features: acute onset, inattention, disorganized thinking, altered level of consciousness, disorientation, memory impairment, perceptual disturbances, psychomotor agitation or retardation, and altered sleep-wake cycle.[16] The CAM can be administered in five minutes and is based on the *Diagnostic and Statistical Manual of Mental Disorders*, Third Edition Revised criteria. It is widely used in the palliative care setting[17,18] and has been validated for this population (sensitivity 0.88 and specificity 1.0).[19] This tool also has been validated in Spanish with a sensitivity of 90%, specificity of 100%, negative predictive accuracy of 97%, and positive predictive accuracy of 100%.[20]

Delirium Rating Scale-Revised-98. This is a 10-item observational scale that rates patients on the characteristic symptoms of delirium: perceptual disturbance, hallucinations, delusions, cognitive status, sleep-wake cycle disturbance, lability, psychomotor behavior, language, and visuospatial ability. The revised version adds three diagnostic items: physical disorder, temporal onset, and fluctuation of symptoms.[21] This tool has been validated in Spanish[22] and is widely used for diagnosis and follow-up, as well as to evaluate the phenomenology of delirium, in palliative care and various other patient populations.[23–25]

Mini-Mental State Examination. The Mini-Mental State Examination (MMSE)[26,27] is a widely used brief objective measure of cognitive function in older adults. It is a 30-item tool that includes tests for orientation, memory, concentration, and visuospatial ability.

MDAS. The MDAS[9] is a 10-item diagnostic and severity assessment questionnaire designed by Breitbart et al. in accordance with the *DSM-IV-TR* criteria for a palliative care population. This scale quantifies severity of delirium and assesses orientation, attention, awareness, short-term memory, digit span, thinking, perceptual disturbance, delusions, psychomotor activity, and sleep-wake cycle disturbance.

Data Collection

Data were collected after delirium was diagnosed following the CAM and clinical assessments of the patients. A first assessment was conducted after informed consent was obtained; when possible, a second assessment was conducted 72 hours later. Each MMSE, Delirium Rating Scale-Revised-98 (DRS-R-98), and MDAS assessment was completed by an attending clinician, research nurse, or psychologist at each center. All researchers participated in a meeting during which instrument use was discussed. Three clinicians, three research nurses, and two psychologists specializing in palliative care and familiar with delirium diagnosis and management conducted the study.

Psychometric Analysis

Reliability. Cronbach's alpha was calculated to assess internal consistency (interitem reliability) among the MDAS items for all 88 subjects. Interobserver reliability was measured by calculating the intraclass correlation coefficient for the ratings of two observers on the MDAS scores for 33 subjects. As delirium intensity changed over time, the two observers assessed patients during a 30-minute period. The mean time of MDAS completion was 10–15 minutes.

Concurrent Validity. Concurrent validity was established by calculating correlation coefficients for the MDAS with DRS-R-98 and

MMSE scales for severity at the baseline 0-hour assessment for all subjects.

Responsiveness. Delirium was assessed at 0 and 72 hours. Changes in MMSE, DRS-R-98, and MDAS findings were compared using correlation and adjusted linear regressions for the 77 subjects who were able to complete both study assessments.

Factor Analysis. Exploratory MDAS factor analysis was performed using an oblique promax rotation to achieve a simple factor structure; this would not be possible using an orthogonal rotation for all subjects.

Sample Size. To establish concurrent validity, 85 patients provide 83% power to show that the correlation between the MDAS and DRS-R-98, and MMSE, is significantly stronger than 0.50, assuming a true correlation of at least 0.70 using a one-sided test of Pearson's r at a significance level of 2.5%. To establish reliability, 88 patients provide 85% power to prove internal consistency is significantly greater than 0.60, assuming a true consistency of at least 0.75 using a one-sided Cronbach's alpha test at a significance level of 2.5%.

Results

The study population comprised 85 patients with advanced cancer and delirium (median age 72 years), 66% of whom were men, with poor performance status; they were mainly bedbound and unable to perform most activities (PPS median 40%). Most patients had multiple causes of delirium (Table 1). Among the subjects, 11 were not able to complete the second assessment for various reasons (one seizure, one panic attack, one death, and eight for unknown reasons).

The MDAS mean ± SD on Day 1 was 11 ± 4 and on Day 3 was 11.5 ± 5. Table 2 describes the delirium-related symptoms in the study population. On Day 1, disorientation (60%), short-term memory impairment (49%), and decreased or increased psychomotor activity (60%) were the more frequent symptoms, presenting with moderate or severe intensity, whereas delusions (13%), perceptual disturbance (20%), reduced level of consciousness (17%), and impaired digit span (24%) were the less frequent symptoms, but presenting as moderate or severe. On Day 3, disorientation was still 60%, moderate or severe short-term memory impairment increased to 58%, and psychomotor activity alteration was present in 58% of the patients; delusions were present in 17%, reduced level of consciousness in 22%, and impaired digit span in 33%.

Table 1
Study Population Characteristics ($N = 85$)

Characteristic	*n*
Median age (IQR)	72 (64–78)
Male, *n* (%)	56 (66)
PPS median (IQR)	40% (40–50)
Cancer diagnosis	
Lung	22
Colorectal	11
Digestive other than colorectal	12
Genitourinary-male	8
Prostate	3
Breast	3
Bladder	3
Endocrine	3
Other	20
Delirium diagnosis	
One cause	12
Multiple causes	73
Infection	37
Organic	51
Metabolic	16
Opioid-induced neurotoxicity	17
Non-opioid psychoactive drugs	18

PPS = Palliative Performance Scale; IQR = interquartile range.

Reliability

The MDAS overall alpha was 0.82, indicating good internal consistency (interitem reliability). Table 3 displays alphas for the Spanish-language MDAS when a given item is removed; the data confirm that no single item has undue influence on the scale (alphas range between 0.78 and 0.82). MDAS Items 1, 2, and 6 in Table 3 contributed most to scale consistency (alpha = 0.78), whereas Items 4 and 10 contributed less (alpha = 0.82). The column "Item Total r" shows an individual item's correlation with the total MDAS score. Strong correlations are defined as higher than 0.7, and moderate correlations are higher than 0.5. According to these criteria, several items showed weak correlations with the total score (Items 4 and 10 in particular). These same items contributed the least consistency to the scale using Cronbach's alpha.

The MDAS's overall intraclass correlation coefficient was 0.95, indicating excellent

Table 2
MDAS Phenomenology: Frequency and Severity of Each Symptom

	Day 1, *n* (%)				Day 3, *n* (%)			
Symptom	None	Mild	Moderate	Severe	None	Mild	Moderate	Severe
Awareness	34 (39)	39 (44)	15 (17)	0 (0)	28 (37)	31 (41)	14 (18)	3 (4)
Disorientation	12 (14)	23 (26)	31 (35)	22 (25)	16 (22)	14 (18)	21 (28)	24 (32)
Memory	24 (27)	21 (24)	29 (33)	14 (16)	9 (12)	23 (30)	27 (36)	16 (22)
Digit span	52 (59)	15 (17)	15 (17)	6 (7)	42 (56)	8 (11)	17 (22)	8 (11)
Attention	11 (13)	39 (44)	35 (40)	3 (3)	12 (16)	34 (45)	24 (32)	5 (7)
Disorganized thinking	29 (33)	33 (38)	22 (25)	3 (4)	23 (31)	29 (38)	14 (19)	9 (12)
Perception	46 (52)	25 (28)	14 (16)	3 (4)	49 (65)	14 (19)	11 (14)	2 (2)
Delusions	67 (76)	10 (11)	8 (9)	3 (4)	57 (75)	6 (8)	9 (12)	4 (5)
Psychomotor activity	5 (6)	30 (34)	50 (57)	3 (3)	7 (9)	25 (33)	39 (51)	5 (7)
Sleep-wake cycle	4 (5)	53 (60)	29 (33)	2 (2)	4 (5)	43 (57)	24 (31)	5 (7)

MDAS = Memorial Delirium Assessment Scale.

interobserver reliability. Good interobserver agreement was displayed for most items; however, Item 10 showed an agreement level considered moderate rather than strong.

Concurrent Validity

The correlation between the MDAS and the DRS-R-98 was $r = 0.80$ (95% CI 0.71, 0.86) using Spearman's rho. A test result showing $r > 0.70$ was significant ($P = 0.0164$) using a one-sided test establishing alpha at 0.025. A test vs. 0.50 was significant at $P < 0.001$. The correlation between the MDAS and the MMSE was $r = -0.74$ (95% CI −0.82, −0.63) using Spearman's rho. A test of $r < -0.70$ was not significant ($P = 0.23$) using a one-sided test establishing alpha at 0.025. A test result of r −0.50 was significant at $P = 0.001$ (Table 4).

Responsiveness

Variation in DRS-R-98 scores correlates with variation in MDAS scores: $r = 0.93$ (95% CI 0.89, 0.95). Testing $r > 0.70$ vs. $r \leq 0.70$ results in $P < 0.001$. Variation in MMSE scores correlates with variation in MDAS scores: $r = -0.84$ (95% CI −0.90, −0.76). Testing $r < -0.70$ vs. $r \geq -0.70$ results in $P = 0.015$ (Table 4). The correlation coefficients and associated *P*-values indicate MDAS strong concurrent validity and responsiveness, as changes in severity detected by the MDAS are detected by the DRS-R-98 and MMSE.

Responsiveness was further explored using multiple linear regression of variation in the MDAS scores vs. variation in the DRS-R-98 and MMSE scores adjusting for sex, diagnosis, and cause of delirium. Variation in DRS-R-98 and MMSE scores was found to be a significant predictor of variation in MDAS scores even after adjustments. A one-point increase in DRS-R-98 variation corresponds to a 0.643-point increase in variation on the MDAS. Patients who had opioid-induced neurotoxicity had a 1.8-point higher MDAS variation than patients who did not have opioid-induced neurotoxicity.

Table 3
Reliability of the MDAS

			Interitem Reliability (Cronbach's alpha = 0.82)		Interobserver Reliability (Overall Intraclass $r = 0.95$)
MDAS Item	Mean	SD	Alpha if Item is Removed	Item Total *r*	Intraclass *r*
1	0.78	.73	0.78	0.66	0.76
2	1.71	1.00	0.78	0.68	0.91
3	1.38	1.05	0.81	0.40	0.78
4	0.72	.99	0.82	0.31	0.88
5	1.35	.75	0.79	0.62	0.84
6	0.99	.86	0.78	0.69	0.85
7	0.70	.86	0.81	0.36	0.88
8	0.41	.80	0.80	0.45	0.70
9	1.57	.66	0.79	0.61	0.87
10	1.34	.61	0.82	0.30	0.66

MDAS = Memorial Delirium Assessment Scale.

Table 4
MDAS Concurrent Validity and Responsiveness

	Concurrent Validity		Responsiveness	
Scale	Spearman's Rho (CI)	P^a	Spearman's Rho (CI)	P^a
DRS-R-98	0.80 (0.71, 0.86)	0.02	0.93 (0.89, 0.95)	<0.001
MMSE	−0.74 (−0.82, −0.63)	0.23	−0.84 (−0.90, −0.76)	0.015

MDAS = Memorial Delirium Assessment Scale; DRS-R-98 = Delirium Rating Scale-Revised-98; MMSE = Mini-Mental State Examination.
[a]In comparison to the null hypothesis with which $P < 0.7$ (DRS-R-98) or $P > -0.7$ (MMSE).

Factor Analysis

A two-factor model was produced. Factor I (neurobehavioral) was represented by MDAS Items 1, 5, 7, 8, 9, and 10 and Factor II (global cognitive) by MDAS Items 2, 3, 4, and 6. Factor loading is interpreted as standardized regression coefficients representing the unique contribution of each factor to the variance of each MDAS item (Table 5).

Finally, concurrent validity was explored for the two MDAS factors determined by factor analysis, not for the entire MDAS scale. Factor I was found to correlate only moderately with the MMSE at −0.56 (−0.69, −0.39), whereas Factor II was found to correlate strongly with the MMSE at −0.81 (−0.87, −0.72). Factor II correlates with the MMSE significantly better than Factor I (rho = 0.7, $P = 0.01$), as illustrated in Table 5.

Discussion

As expected, the MDAS has demonstrated strong responsiveness to delirium changes. According to our data, this scale has two factor loadings: neurobehavioral and global cognitive. This study also has produced the first Spanish version of the most specific questionnaire to evaluate delirium in palliative care and cancer patients and evaluated the psychometric characteristics of the instrument in a cancer population. The Spanish version of this questionnaire will be of clinical utility in all Spanish-speaking countries and in the U.S., where Hispanics are the fastest growing population.[28]

The MDAS has been used to assess the efficacy of different antipsychotics.[29,30] In this study, the tool strongly correlated with changes in delirium severity as assessed by the DRS-R-98 and MMSE. This indicates the good responsiveness to changes in delirium severity of this instrument. The MDAS also demonstrates good concurrent validity, strongly correlating with the DRS-R-98 and MMSE.[9,11,12] The MDAS is a useful delirium assessment questionnaire that measures delirium intensity, is sensitive to changes in delirium severity, and can be used with a high degree of accuracy by a variety of professionals.

The Spanish version of the MDAS demonstrated a similar consistency and reliability observed in other studies and languages.[9–11] This tool has a high degree of internal consistency

Table 5
Factor Pattern MDAS Loadings

	Rotated Factor Pattern (Standardized Regression Coefficients)	
MDAS Item	Factor I, Neurobehavioral	Factor II, Global Cognitive
1. Reduced awareness	**0.52***	0.32
2. Disorientation	0.31	**0.54***
3. Short-term memory	−0.17	**0.70***
4. Impaired digit span	−0.20	**0.63***
5. Reduced attention	**0.67***	0.14
6. Disorganized thinking	0.32	**0.53***
7. Perceptual disturbance	**0.54***	−0.11
8. Delusions	**0.60***	−0.08
9. Psychomotor activity	**0.87***	−0.11
10. Sleep-wake cycle	**0.47***	−0.10
Correlation		Rho = 0.7 ($P = 0.01$)
MMSE	−0.56	−0.81

MDAS = Memorial Delirium Assessment Scale; MMSE = Mini-Mental State Examination.
Items in bold or with asterisks are related.

and was rated with high levels of inter-rater reliability between raters in different settings. The MDAS delirium diagnosis differs according to the different populations and places of care; [9,10]this occurs with other screening tools as well, such as the MMSE.[26] In this study, as we have focused on advanced cancer patients with delirium, we have assumed a score of 7 as the screening cut-point.[10]

Breitbart et al.[9] suggested that factor analysis could help to categorize delirium subtypes based on MDAS item profiles. The main factor assessed by the MDAS is delirium, with interitem reliability of 0.82 (Cronbach's alpha) in this study. Corroborating the findings of Lawlor et al.,[10] we have identified two main factor loadings: global cognitive factors that include disorientation, short-term memory impairment, impaired digit span, and disorganized thinking, and neurobehavioral factors that include reduced awareness, reduced attention, perceptual disturbance, delusions, altered psychomotor activity, and sleep-wake cycle disturbances. In our study, reduced awareness and attention are considered neurobehavioral factors. Lawlor et al. regarded these items as global cognitive factors, but they also found that these symptoms correlated to neurobehavioral factors. According to the *DSM-IV-TR* delirium criteria, these two items are the A criteria (not related to cognition). In a more in-depth interpretation of factor loadings described in this study, our data identified a significant statistical relationship when comparing the factor models with those of the MMSE. Factor II (global cognitive) more strongly correlates with the MMSE than Factor I (neurobehavioral) (Table 5). The differences between our data and those found in the Lawlor et al. study exist because we have conducted our analysis in a population with delirium, and the MMSE was completed at the same time as the MDAS. Because Lawlor et al. completed the MMSE at different times than the MDAS, fluctuations in delirium could bias their analysis.

Grassi et al.[11] identified two main areas, one related to the failure of the arousal mechanism (digit span, disorientation, attention, psychomotor activity, awareness, short-term memory, and sleep-wake cycle disturbance) and the other related to the onset of positive phenomena affecting perception (delusions, perceptual disturbance, and disorganized thinking). Our findings showed a stronger association of delusions and perceptual disturbance with neurobehavioral alterations than with cognitive impairment.

According to data obtained in this study, the MDAS can measure alterations in behavior produced by delirium. Additional research on this topic is necessary and could lead to the development of two MDAS subscales, which could be of clinical use in the treatment of the most distressing neurobehavioral delirium symptoms. The neurobehavioral alterations associated with delirium are especially distressing for patients and their caregivers.[6,31,32]

The main limitation of this study is the fact that the same clinician completed all the instruments; this could bias the study's concurrent validity, especially of the DRS-R-98, which explores similar concepts. Analyzing this psychometric characteristic was not the main objective of this study, and the concurrent validity of the MDAS has already been well analyzed and reported. However, we have found similar data in other studies, and the assessments in this study were done by different health professionals, working in three different settings; therefore, we can argue that our data do not represent the interpretation of a single professional. In our opinion, because the MMSE is completed by patients and the MDAS by health professionals, completion of both tools by the same researcher at the same time does not bias the factor analysis and does not allow symptom fluctuations to alter the results, as could have happened in the Lawlor et al. study.

The MDAS has shown good responsiveness, which confirms its capacity for monitoring delirium assessment. Two differentiated factor loadings suggest the potential use of MDAS subscales. It is necessary to explore the value of potential MDAS subscales that would assess neurobehavioral and global cognitive factors. Future studies should determine the receiver-operating characteristic curve for the MDAS in different patient populations, because the cut-points will likely be different according to the patient characteristics and the setting of care.[9,10]

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