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Original Study

Visual and Hearing Impairment Are Associated With Delirium in Hospitalized Patients: Results of a Multisite Prevalence Study

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A B S T R A C T

Objective: Sensory deficits are important risk factors for delirium but have been investigated in single-center studies and single clinical settings. This multicenter study aims to evaluate the association between hearing and visual impairment or bi-sensory impairment (visual and hearing impairment) and delirium.
Design: Cross-sectional study nested in the 2017 "Delirium Day" project.
Setting and Participants: Patients 65 years and older admitted to acute hospital medical wards, emergency departments, rehabilitation wards, nursing homes, and hospices in Italy.
Methods: Delirium was assessed with the 4AT (a short tool for delirium assessment) and sensory deficits with a clinical evaluation. We assessed the association between delirium, hearing and visual impairment in multivariable logistic regression models, adjusting for: Model 1, we included predisposing factors for delirium (ie, dementia, weight loss and autonomy in the activities of daily living); Model 2, we added to Model 1 variables, which could be considered precipitating factors for delirium (ie, psychoactive drugs and urinary catheters).
Results: A total of 3038 patients were included; delirium prevalence was 25%. Patients with delirium had a higher prevalence of hearing impairment (30.5% vs 18%; $P < .001$), visual impairment (24.2% vs 15.7%; $P < .01$) and bi-sensory impairment (16.2% vs 7.5%) compared with those without delirium. In the multivariable logistic regression analysis, the presence of bi-sensory impairment was associated with delirium in Model 1 [odds ratio (OR) 1.5, confidence interval (CI) 1.2–2.1; $P = .00$] and in Model 2 (OR 1.4; CI 1.1–1.9; $P = .02$), whereas the presence of visual and hearing impairment alone was not associated with delirium either in Model 1 (OR 0.8; CI 0.6–1.2, $P = .36$; OR 1.1; CI 0.8–1.4; $P = .42$) or in Model 2 (OR 0.8, CI 0.6–1.2, $P = .27$; OR 1.1, CI 0.8–1.4, $P = .63$).

The authors declare no conflicts of interest.

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Conclusions and implications: Our findings support the importance of routine screening and specific interventions by a multidisciplinary team to implement optimal management of sensory impairments and hence prevention and the management of the patients with delirium.

Delirium is an acute brain dysfunction characterized by inattention and impaired awareness with fluctuations.[1] It affects on average 1 of 5 hospitalized older patients.[2] Its prevalence is even higher when it occurs in the context of dementia, ranging from 22% to 89%.[3] The occurrence of delirium is linked to adverse outcomes, including cognitive and functional impairment, and increased mortality, length of stay, and health care costs.[4–9] Delirium has also been described to be distressing for patients, caregivers, and health care providers.[10,11] Delirium subtypes vary according to different studies and also according to the presence of dementia. A recent large cohort of patients with dementia reported the hyperactive form being the most frequent, followed by the hypoactive, mixed, and nonmotor subtype.[12]

It is now recognized that delirium can be prevented in 30% of the patients with a multicomponent and multidisciplinary intervention.[13,14] Twenty years ago, Inouye and colleagues[15] published a seminal paper underlying the importance of focusing on cognitive stimulation, sleep deprivation, immobility, dehydration, and sensory impairments (ie, visual and hearing impairments). In previous years, it has been shown that visual impairment is a significant predisposing risk factor for delirium and the coexistence of this sensory deficit with a severe illness, dehydration, and cognitive impairment acted with an almost multiplicative effect to increase the delirium risk.[16] Since then, few studies have been published investigating the visual impairment and hearing impairment as risk factors for delirium in patients admitted to medical and hospice wards, and emergency departments.[17–21]

It is well known how the risk of hearing and vision impairment increases with age.[22] In addition, given the growing proportion of older persons and the future increase of dementia prevalence, it is expected to have a higher than current number of people with cognitive impairment and sensory deficits.[23] Hearing impairment accounts for 9% of the burden of dementia, and is considered as a modifiable risk factor to be assessed in the older patients.[24] The link between cognitive impairment and visual and hearing impairment is complex. Indeed, visual impairment could affect cognitive function, but altered cognition could also affect vision.[25,26] Similarly, older persons with hearing impairment have higher risk of cognitive impairment than those without.[27] In addition, the dual sensory impairment can increase the development of behavioral symptoms in persons with dementia.[28] Given the importance of the relationship between sensory impairments and cognitive deficits, the American Geriatrics Society and the National Institute on Aging Bench-to-Bedside conference focused specifically on the current knowledge and on identifying research questions on this specific topic to improve outcomes of the growing older population.[29]

In 2017, a multicenter point-prevalence study named "Delirium Day" was conducted in Italy to evaluate the prevalence of delirium among patients admitted to different health care settings. As part of the study protocol, the presence of visual and hearing impairment was recorded. The aims of the current study are (1) to determine if there is an independent association between prevalence of visual and hearing impairment and prevalence of delirium; and (2) to investigate if patients with bi-sensory impairment (visual and hearing impairment) are more likely to have delirium, compared with single visual or hearing impairment and with patients without a sensory impairment.

Methods

This is a cross-sectional study nested in the "Delirium Day" study. The aims of the "Delirium Day" were previously described.[30] The "Delirium Day" study is a nationwide point-prevalence study conducted in Italy evaluating the prevalence of delirium on an index day; 3 editions (2015, 2016, 2017) have been carried out. In this study we include only the data from the 2017 edition because in the previous editions (2015, 2016) we did not record the presence of sensory deficits. The study protocol was approved by the local ethical committee. Each patient 65 years and older admitted, on the index day, in acute hospital medical wards, emergency department, rehabilitation wards, nursing homes, and hospice was enrolled after obtaining an informed consent. The next of kin signed the informed consent when the participants were not capable because of delirium or dementia. Exclusion criteria were study refusal, severe visual impairment and deafness, aphasia, coma.

Delirium Evaluation

Each patient was assessed for the presence of delirium by the attending physician using the 4AT. A 4AT score $\geq$4 was used to diagnose delirium. The 4AT has been originally validated in Italian acute geriatric and rehabilitation wards showing a sensitivity of 89.7% and a specificity of 84.1% against a DSM-IV-TR evaluation as a reference standard.[31] A recent large multicenter study of older acute medical inpatients showed the 4AT had a sensitivity of 76% and a specificity of 94%, with a receiver operating characteristic curve of 0.90.[32] A 4AT score of 0 suggests the absence of dementia or delirium, a score between 1 and 3 suggests a possible cognitive impairment but not delirium, and a score $\geq$4 is strongly suggestive of delirium. A subanalysis of the 4AT in patients with dementia showed a sensitivity of 94% and a specificity of 64.9% for delirium detection.

Sensory Deficit Evaluation

Visual impairment was diagnosed when a patient was unable to see the fingers of the interviewer at 1 meter of distance during daylight with or without aids. Hearing impairment was diagnosed when a patient was unable to understand the interviewer's words at a normal voice volume at distance of 1 meter with or without aids. These types of assessment for sensory deficits have been previously used.[33,34] When the bedside assessment of the sensory impairments was not feasible due to the patient's attention deficit or behavioral symptoms, each impairment was considered present when a previous diagnosis of visual or hearing deficit was present in the clinical history of the patient.

Clinical Assessment

Demographics were recorded. Functional status was evaluated assessing the independence of the patient for the activities of daily living during the 15 days before the hospital admission for the acute, rehabilitation, and hospice wards, and 15 days before the index evaluation for nursing home patients. The ability to dress, feed, and manage their medication was evaluated as follows: each item is given

a score of 1 if the person is dependent in the activity and a score of 0 if the person is independent in the activity. An autonomy score is calculated as the sum of 3 items, ranging from 0 (being independent) to 3 (being totally dependent). The new mobility score (NMS), also used to evaluate the functional status,[35] is a composite score of the patient's ability to perform indoor walking, outdoor walking, and shopping, before the index hospitalization for the acute, rehabilitation, and hospice wards, and 15 days before the index evaluation for nursing home patients, providing a score between 0 and 3 (0: not at all, 1: with help from another person, 2: with an aid, 3: no difficulty) for each function, resulting in a total score from 0 to 9, with 9 indicating a high prehospitalization functional status. History of falls and weight loss (>5%) in the 12 months before the index day evaluation were also recorded. The presence of dementia was defined by a documented diagnosis in the medical records and/or prescription of Acetylcholinesterase inhibitors (AChE-I) or memantine before admission.

The presence of comorbidity was defined with the Charlson index,[36] excluding dementia from the total score because we analyzed the variable dementia separately in the statistical analysis. The presence of psychoactive drugs (ie, antipsychotics, benzodiazepines, antidepressants) received by each patient on the index day was recorded. We also collected, on the index day, information on the use of peripheral venous catheters and urinary catheters.

Statistical Analysis

Quantitative variables were reported as mean and standard deviation (SD) and qualitative variables as count and percentages. The *t*-test was used to compare quantitative variables between patients with and without delirium, and the χ^2 or Fisher exact test were used to compare qualitative variables between the 2 group of patients. When comparing patients without sensory deficits, with visual or hearing impairment, and with bi-sensory impairment. A 1-way analysis of variance has been performed for quantitative variables.

Multivariable logistic regression was used to test the association between the presence of sensory deficits and delirium, adjusting for other clinical risk factors and using as the reference group patients without visual or hearing impairment. Variables were included in the models if they were statistically significantly different in the univariate analysis with a P value $\leq .05$. We built 2 multivariable logistic regression models. In Model 1 we included baseline variables, which could act as predisposing factors for delirium (ie, dementia, autonomy score, weight loss in the 12 months before the index evaluation). In Model 2 we also added variables that could be considered precipitating factors for delirium (ie, psychoactive drugs and urinary catheters). Results were presented as adjusted odds ratios (ORs) and their 95% confidence interval (CI). Statistical analyses were performed with the statistic "R" software (R version 3.6.1, 2019–07–05, Copyright 2015 The R Foundation for Statistical Computing).

Results

A total of 3038 patients were included; 1535 from acute medical wards, 130 from the emergency department, 620 from rehabilitation wards, 667 from nursing homes, and 82 from hospice (Appendix 2).

The overall prevalence of visual impairment was 17.9% and hearing impairment 21.2%. The bi-sensory impairment was present in 9.7% of the population. Overall delirium prevalence was 25.5%. Patients with delirium had a higher prevalence of hearing impairment (30.5% vs 18%), visual impairment (24.2% vs 15.7%) and bi-sensory impairment (16.2% vs 7.5%) compared with those without delirium (Table 1). Overall, patients with delirium had a greater prevalence of dementia (66.9% vs 19.2%), with more severe comorbidity as indicated by the Charlson Index (3.6 ± 2.9 vs 3.2 ± 2.9), more common history of falls (41.2% vs 33.3%) and weight loss (32.1% vs 21.7%) in the year before the index day evaluation. In addition, patients with delirium had worse functional status before the index day of evaluation, as indicated by the autonomy score (2.1 ± 1.0 vs 1.0 ± 1.0) and the NMS (1.6 ± 1.7 vs 2.7 ± 1.8). The prevalence of delirium was found to be higher in nursing homes (32.3%) and hospice units (37.8%) followed by medical (24.5%) and rehabilitation wards (20.5%), and emergency departments (19.2%).

In the univariate analysis, there was a "dose-effect" association between the absence of sensory deficits, the presence of visual or hearing impairment or bi-sensory impairment, and the prevalence of delirium (22.2%, 25%, 31.8%, and 42.5%, respectively) and dementia (26.5%, 36.3%, 41.5% and 51%) (Table 2). In addition, patients with bi-sensory impairment, compared with patients with a single deficit and no deficits, had higher prevalence of weight loss in the year before the hospital admission (23.6%; 23.4%; 24.8%; 28.7%) and a worse functional status as indicated both by the autonomy score and the NMS.

In the multivariable logistic regression analysis, the presence of bi-sensory impairment was associated with delirium in Model 1 (OR 1.5; CI 1.2–2.0; $P = .00$) and in Model 2 (OR 1.4; CI 1.1–1.9; $P = .02$) (Table 3) while the presence of visual and hearing impairment alone was associated with delirium neither in Model 1 (OR 0.8; CI 0.6–1.2, $P = .36$; OR 1.1; CI 0.8–1.4; $P = .42$) nor in Model 2 (OR 0.8; CI 0.6–1.2, $P = .27$; OR 1.1; CI 0.8–1.4, $P = .63$). In all 2 models other variables associated with delirium were dementia (OR 5.9; CI 4.8–7.2, $P = .00$; OR 6.1; CI 4.9–7.4, $P = .00$), worse functional status as indicated by the autonomy score (OR 2.9; CI 2.2–3.8, $P = .00$; OR 2.6; CI 1.9–3.4, $P = .00$; OR 2.2; CI 1.7–3.0, $P = .00$), greater loss of weight in the year before the index evaluation (OR 1.7; CI 1.4–2.1, $P = .00$; OR 1.7; CI 1.3–2.1, $P = .00$). In Model 2 we also found an association between delirium, psychoactive drugs (OR 1.4; CI 1.1–1.7, $P = .00$), and urinary catheters (OR 2.1 CI 1.7–2.6, $P = .00$). In Model 1 we also tested for an interaction

Table 1
Patients' Characteristics According to the Presence of Delirium

Variables	Delirium Yes n = 776	Delirium No n = 2262	*P* Value
Age, y	84.7 ± 7.1	82.2 ± 7.6	<.001
Gender (female)	488 (62.9)	1378 (60.9)	.353
Visual impairment	188 (24.2)	356 (16)	<.001
Hearing impairment	237 (31)	408 (18)	<.001
Hearing and visual impairment	126 (16.2)	170 (7.5)	<.001
Dementia	519 (66.9)	435 (19.2)	<.001
Charlson Index	3.6 ± 2.9	3.2 ± 2.9	<.001
At least 1 fall in the past 12 months	320 (41.2)	754 (33.3)	<.001
Weight loss in the past 12 months (>5%)	249 (32.1)	490 (21.7)	<.001
Autonomy score*	2.1 ± 1	1 ± 1	<.001
New mobility score	1.6 ± 1.7	2.7 ± 1.8	<.001
Psychoactive drugs†	474 (61.1)	1008 (44.6)	<.001
Urinary catheters	270 (34.8)	470 (20.8)	<.001
Ward type			<.001
Medical ward	376 (48)	1159 (51)	
Emergency department	25 (3)	105 (5)	
Rehabilitation	127 (16)	493 (22)	
Nursing home	217 (27.9)	454 (21)	
Hospice	31 (4)	51 (2)	

Data are reported as mean (SD) or n (%).

*Autonomy score was defined as the sum of the score in the following items: (1) Ability in dressing; (2) ability in feeding; (3) ability in medication management. For each item is given a score of 1 if the person is dependent in the activity and a score of 0 if the person is independent in the activity. The score ranges from 0 (being independent) to 3 (being totally dependent).

†Psychoactive drugs include the following: Benzodiazepine short-acting, Benzodiazepine intermediate-acting, Benzodiazepine long-acting, Antidepressants selective serotonin reuptake inhibitor, Antidepressants serotonin norepinephrine reuptake inhibitor, Tricyclic antidepressants, atypical antidepressants, typical and atypical antipsychotics

Table 2
Patients' Characteristics According to the Presence of Hearing and Visual Impairments

Variables	None, n = 2145	Visual Impairment, n = 248	Hearing Impairment, n = 349	Visual and Hearing Impairment, n = 296)	*P* Value
Age, y	81.5 ± 7.5	83.6 ± 7.2	86.2 ± 6.4	82.8 ± 7.6	<.001
Gender (female)	1262 (58.8)	178 (72)	216 (62)	210 (71)	<.001
Delirium	477 (22.2)	62 (25)	111 (31.8)	126 (42.5)	<.001
Dementia	685 (26.5)	90 (36.3)	145 (41.5)	151 (51)	<.001
Charlson Index	3.2 ± 2.8	3.3 ± 3.4	3.8 ± 3.1	3.5 ± 2.3	.02
At least one fall in the last 12 months	726 (33.8)	98 (39.5)	142 (40.7)	108 (36.5)	.046
Weight loss in the last 12 months (>5%)	508 (23.6)	58 (23.4)	90 (25.8)	85 (28.7)	.333
Autonomy score*	1.1 ± 1.1	1.6 ± 1.1	1.6 ± 1.1	2 ± 1	<.001
New Mobility Score	2.5 ± 1.9	2.4 ± 1.8	2.2 ± 1.7	1.8 ± 1.7	<.001
Psychoactive drugs†	1004 (47)	134 (54)	175 (50)	169 (57)	.002
Urinary catheters	472 (22)	59 (24)	111 (31.8)	98 (33)	<.001

Data are reported as median/mean (SD/interquartile range) or n (%)

*Autonomy score was defined as the sum of the score in the following items: 1) Ability in dressing; 2) ability in feeding; 3) ability in medication management. For each item is given a score of 1 if the person is dependent in the activity and a score of 0 if the person is independent in the activity. The score ranges from 0 (independent) to 3 (dependent).

†Psychoactive drugs include the following: Benzodiazepine short-acting, Benzodiazepine intermediate-acting, Benzodiazepine long-acting, Antidepressants selective serotonin reuptake inhibitor, Antidepressants serotonin norepinephrine reuptake inhibitor, Tricyclic antidepressants, atypical antidepressants, typical and atypical antipsychotics.

between dementia and sensory deficits, without finding a statistically significant association (results not reported).

Discussion

This is the first multicenter study to specifically investigate the association between visual and hearing impairments with delirium in a large population of older patients admitted to different clinical settings. Overall, we found a relatively high prevalence of hearing and visual impairment. Patients with delirium had a higher prevalence of sensory deficits. In the multivariable analysis, the dual sensory impairment was statistically associated with delirium both in Model 1 and Model 2.

In the United States, the overall prevalence of hearing impairment in the community increases from 29.3% in persons 60 to 69 years of age up to 79% in persons 80 years and older.[37] The prevalence of visual impairment is lower, with 6% in persons 60 to 69 years of age and up to 7% in persons 80 years of age and older. Another study reported visual impairment in 14.4% of community-dwelling Japanese older persons, and hearing impairment in 23.3%.[38] In a cohort of older patients with hip fracture admitted to a geriatric ward, Grue et al.[39] reported that 16% of the patients had no sensory impairments, 15.4% had visual impairment, 38.6% had hearing impairment, and 30.1% had bi-sensory impairment. A recent systematic review described the dual sensory impairment with a prevalence ranging from 3% in those aged 60 to 69 years to 21.9% in those aged 80 years and older.[40] We found a relatively high prevalence of visual and hearing impairment, compared with previous studies, but a dual sensory impairment prevalence in line with previous investigations cited previously.

Previous studies have investigated the association between visual and hearing impairment and delirium in different settings. A systematic review reported hearing and visual impairment were moderate risk factors for delirium with a combined OR of 1.9 (95% CI 1.4–2.6) and 1.7 (95% CI 1.2–2.3).[20] Similar results on visual impairment (OR 1.89; 95% CI 1.03–3.47) were also reported in a more recent systematic review and meta-analysis.[41] However, this evidence is supported by single-center studies with a relatively small sample sizes. Subsequent studies focused on the association between delirium and sensory impairments in older patients admitted to the emergency department[19] and more recently specifically in the context of palliative care settings and burn centers.[18,42] In our study, we found a statistically significant association only between delirium and the presence of dual impairment. This might be explained by the fact that persons with dual impairment had a higher prevalence of dementia, worse functional status at baseline, and greater odds of weight loss in

Table 3
Association Among Visual Impairment, Hearing Impairment, and Delirium*

Variables	Model 1		Model 2	
	Odds Ratio (Confidence Interval)	*P* Value	Odds Ratio (Confidence Interval)	*P* Value
No visual or hearing impairment	Ref		Ref	
Visual impairment	0.8 (0.6–1.2)	.36	0.8 (0.6–1.2)	.27
Hearing impairment	1.1 (0.8–1.4)	.42	1.1 (0.8–1.4)	.63
Visual and hearing impairment	1.5 (1.2–2.1)	.00	1.4 (1.1–1.9)	.02
Dementia	5.9 (4.8–7.2)	.00	6.1 (4.9–7.4)	.00
Autonomy score†	2.9 (2.2–3.8)	.00	2.6 (1.9–3.4)	.00
Weight loss in the past 12 months (>5%)	1.7 (1.4–2.1)	.00	1.7 (1.3–2.1)	.00
Psychoactive drugs‡	—	—	1.4 (1.1–1.7)	.00
Urinary catheters	—	—	2.1 (1.7–2.6)	.00

*In Model 1, we included baseline variables, which could act as predisposing factors for delirium. In Model 2, we added variables, that could be considered precipitating factors for delirium (ie, psychoactive drugs and urinary catheters).

†Autonomy score was defined as the sum of the score in the following items: (1) Ability in dressing; (2) ability in feeding; (3) ability in medication management. For each item is given a score of 1 if the person is dependent in the activity and a score of 0 if the person is independent in the activity. The score ranges from 0 (independent) to 3 (dependent).

‡Psychoactive drugs include the following: Benzodiazepine short-acting, Benzodiazepine intermediate-acting, Benzodiazepine long-acting, Antidepressants selective serotonin reuptake inhibitor, Antidepressants serotonin norepinephrine reuptake inhibitor, Tricyclic antidepressants, atypical antidepressants, typical and atypical antipsychotics.

the year before the index day evaluation, an indirect sign of frailty. These findings are indeed interesting and worth discussing because several studies have reported the association between sensory deficits and dementia, worse functional status, and higher risk of falls.[43–45] This might indirectly explain how sensory deficits might amplify the risk of adverse outcomes related to delirium, such as cognitive and functional decline and higher risk of falls.

Approximately 20 years ago, Inouye and colleagues[15] underlined the importance of assessing the patients for the presence of visual and hearing impairment, providing them with glasses and hearing aids if needed. This approach has been proven to be effective for delirium prevention. Indeed, the recently published Scottish delirium guidelines strongly emphasize the importance of delirium risk reduction with a multidisciplinary approach that includes early mobilization, pain control, promotion of sleep hygiene, maintaining hydration and nutrition, providing orientation, and ensuring that patients have their glasses and hearing aids.[46,47] Even the World Health Organization (WHO) Guidelines on Integrated Care for Older People (ICOPE) strongly recommends for the evaluation and management of visual and hearing impairments.[48] To warrant a proper use of glasses and hearing aids, the intervention of nurses or occupational therapists (OTs) should be considered. Nurses are involved in the everyday assistance of the patient at risk of delirium whereas OTs are specialists in restoring the patient's independence in basic and instrumental activities of daily living, on the basis of patient's preferences.[49] For example, Alvarez and colleagues[50] recently reported the results of a feasibility study promoting the previously mentioned intervention with technology in older patients admitted to acute hospital wards. The intervention includes different activities via the interaction with a tablet, which prompt the patient to wear glasses and hearing aids.

As Inouye[16] described in the past, there are predisposing and precipitating factors for delirium. We decided to approach the statistical analysis using 2 statistical models including in Model 1 baseline variables, which could act as predisposing factors for delirium (ie, dementia, weight loss, and autonomy in the activities of daily living); in Model 2 variables, which could be considered precipitating factors for delirium (ie, psychoactive drugs and urinary catheters). Given the point-prevalence nature of the study we cannot rule out causality, although for Model 1 we were able to select variables that described the prehospitalization patient's condition. It is likely that urinary catheters and psychoactive drugs, included in Model 2, are newly placed and prescribed during the hospitalization. When considering possible interventions for delirium prevention, clinicians and researchers may divide risk factors according to the amenability to interventions. Indeed a multidisciplinary team can intervene on use of psychoactive drugs, urinary catheters, and provide interventions on visual and hearing impairment, including visual aids (eg, glasses or magnifying lenses), adaptive equipment (eg, fluorescent tape on call bell), amplifying devices, and careful communication techniques.[16] Conversely, other factors, such as weight loss or functional impairment before the index hospitalization, are unlikely to be modified. Predisposing factors such as dementia might be considered partially amenable to interventions, as, if it is correctly identified, a personalized management may be adopted to reduce the deleterious effect of the environment, such as the "This is me" approach, as suggested by the Royal College of Nursing in collaboration with the UK Alzheimer Society (alzheimers.org.uk/thisisme).

Our study presents strengths and limitations. To the best of our knowledge, this is the first multicenter real-world study showing the association of dual sensory impairment with delirium in a large population of older patients admitted to different clinical settings. We were unable to evaluate the degree of the visual and hearing impairment as well as the degree of correction by means of sensory aids, which could further explain the findings of the lack of the association of delirium with the single sensory impairment.

Conclusions and Implications

Our findings support the importance of routine screening for sensory impairments by a multidisciplinary team to prompt the necessary appropriate measures/interventions to improve the management of patients with delirium across different clinical settings. It should be noted that the type of assessment of sensory impairment used in this study was simple and easy to use, increasing the daily use at the patient's bedside.

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Supplementary Data

Supplementary data related to this article can be found online at https://doi.org/10.1016/j.jamda.2020.03.009.

Author Contribution: design (Morandi, Inzitari, Udina, Gual, Cherubini, Mossello, Marengoni, Bellelli); methods (all authors), subject recruitment (Morandi, Inzitari, Udina, Gual, Cherubini, Gentile, Mossello, Marengoni, Olivé, Riba, Ruiz, de Jaime, Bellelli and authors indicated in Appendix 1), data collections (Morandi, Inzitari, Udina, Gual, Cherubini, Gentile, Mossello, Marengoni, Olivé, Riba, Ruiz, de Jaime, Bellelli and authors indicated in Appendix 1), analysis and preparation of paper (all authors).

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