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# The Phenomenology of Delirium and its Motoric Subtypes in Patients with Cancer

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## Abstract

*Aim: To examine the phenomenological characteristics of delirium and its motoric subtypes in patients with cancer based on the Memorial Delirium Assessment Scale (MDAS) items.*
*Methods: We conducted a secondary analysis of our delirium database. Sociodemographic as well as medical variables, the MDAS subitems (1-10) and the Karnofsky Performance Status scale (KPS) were analyzed in respect to the phenomenology of delirium.*
*Results: We were able to retrieve 111 cases with diverse cancer diagnoses from our delirium database. The mean age of all subjects was 65.6 years, the delirium severity as measured with the MDAS was 18.3. The most common and severe symptoms were found in the cognitive domain (71-90%, MDAS 1.96-2.35), psychomotor abnormality (95%, MDAS 2.14), sleep-wake cycle disturbance (87%, MDAS 1.97) and disturbance of consciousness (87%, MDAS 1.94). Concentration was the most impaired cognitive task. Hyperactive delirium in comparison to hypoactive delirium was more severe; domains of more severe impairment were cognition, level of organization, perception, and psychomotor behavior. The prevalence of disorganization, perceptual disturbances and delusions were increased in hyperactive delirium, but in particular perceptual disturbances and delusions also occurred to a substantial rate in hypoactive delirium (59.5 and 53.2%). Perceptual disturbances and delusions were not associated with the impairment of the cognitive domain.*
*Conclusion: Delirium in cancer patients is a disorder of cognition, consciousness, psychomotor behavior and sleep-wake cycle. Hyperactive delirium may present more severe, and the severity of symptomatology in the cognitive domain, level of organization, perception and psychomotor behavior may be increased. Perceptual disturbances and delusions may occur to a substantial rate in hypoactive delirium (German J Psychiatry 2011; 14(2): 66-71).*

*Keywords: Delirium, phenomenology, subtypes, perceptual disturbances, delusions*

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## Introduction

Delirium is a neuropsychiatric disorder, which is characterized by disturbances of consciousness, attention, cognition and perception with an abrupt onset and fluctuating course and usually has an underlying physiological etiology (Trzepacz et al., 1999). Other frequent symptoms of delirium include various mood changes, sleep-wake cycle disturbances, psychomotor as well as language abnormalities (Meagher et al., 2000).

The phenomenology of delirium has been examined in a number of studies. In a review Turkel et al. (2006) found the arousal disturbance in 75% (48-82%), impaired orientation in 76% (62-100%), impaired attention in 65% (17-100%), impaired memory in 84% (64-100%), disturbance in thought process in 48% (2-68%), perceptual disturbances in 33% (20-78%), delusions in 27% (19-68%), psychomotor retardation in 59% (53-60%), psychomotor agitation in 44% (28-90%) and sleep-wake cycle disturbances in 53% (18-98%).

The prevalence of perceptual disturbances and delusions was further studied by Cutting (1987), revealing approximately equal prevalences of perceptual disturbances and delusions

(47.3 and 51.4%). Webster (2000) found a prevalence of 32.6% perceptual disturbances, 25.6% delusions and 15.8% both perceptual disturbances and delusions.

Meagher et al. (2007) focused on cognitive and non-cognitive symptoms of delirium and found that inattention and sleep-wake cycle disturbance were most frequent, while disorientation was the least frequent cognitive deficit. In this study perceptual disturbances and delusions were not associated with cognitive deficits.

Delirium is classified into subtypes based on arousal disturbance and motoric change. Lipowski was the first to identify delirium subtypes based on levels of alertness (Lipowski, 1983). The formal definitions of these subtypes were hypoalert-hypoactive and hyperalert-hyperactive (Lipowski, 1989). By contrast, O'Keeffe and Meagher based their classification of delirium on motoric change (O'Keeffe & Lavan, 1997; O'Keeffe, 1999; Meagher et al., 2008; Meagher et al., 2000; Meagher et al., 2008; Meagher & Trzepacz, 2000). Besides hypoactive and hyperactive delirium a third subtype, the mixed subtype has been described, featuring delirium with both hypoactive and hyperactive symptoms (Koponen et al., 1989; Liptzin & Levkoff, 1992; Meagher et al., 1996).

Several studies have previously sought to describe differences in frequency and phenomenology between the subtypes. The main studies evaluating the subtypes of delirium (Stagno et al., 2004) found a prevalence of 15-79% for the hypoactive type, 6-46% for the hyperactive type and 11-55% for the mixed type. Because different studies used a variety of definitions for delirium subtypes, it is difficult to compare findings of different authors.

Regarding differences in phenomenology between hypoactive and hyperactive delirium, Ross found that perceptual disturbances such as hallucinations and delusions are significantly more common in hyperactive delirium (67 and 50%) than in hypoactive delirium (3% each) among patients with worsened arousal disturbance (Ross et al., 1991).

We performed a secondary analysis of our delirium database in respect to the MDAS subitems in order to further assess the phenomenology of delirium and in particular examine the phenomenology of the motoric subtypes of delirium.

# Methods

## Subjects and Procedures

Subjects in this analysis included patients referred for delirium management to the Memorial Sloan Kettering Cancer Center (MSKCC) Psychiatry Service from July 2004 to June 2006. Clinical data, including serial MDAS ratings, etiologies of delirium, medications and dosages utilized, adverse events and co-morbid medications as well as medical conditions were recorded in an Institutional Review Board (IRB) - approved MSKCC Psychiatry Service clinical database.

Inclusion criteria were broad, meeting the DSM-IV-TR (American Psychiatric Association, 2000) criteria for delirium, only cases with delirium due to general medical condition were included. Exclusion criteria were objections on the side of the patient or family to be evaluated for delirium, inability to comply with delirium rating, severe agitation, critical medical condition and imminent death. Delirium secondary to substance intoxication and withdrawal was excluded. All patients and families gave verbal consent to being evaluated for delirium. In patients with limited capacity to provide consent due to delirium, the patient's primary caregiver provided verbal consent to the patient's assent to treatment.

We conducted a secondary analysis of our delirium database focusing on the Memorial Delirium Assessment Scale (MDAS) items representing the phenomenology of delirium. Scale items assess disturbance in arousal and level of consciousness as well as several areas of cognitive functioning (memory, attention, orientation, and disturbances in thinking), psychomotor activity and sleep-wake cycle disturbance. Symptoms can be rated as absent (0), mild (1), moderate (2) and severe (3) on the MDAS. Subtyping of delirium in the MDAS is based on the motoric subtype (Meagher et al., 2008; Meagher et al., 2000; Meagher et al., 2008). Further scales used were the Karnofsky Scale of Performance Status (KPS) (Karnofsky & Burchenal, 1949) indicating physical performance ability.

## Statistical Analysis

Analyses were performed with the SPSS 16 statistical software package for Windows. In the first step descriptive analysis was used to compute the severity of symptomatology represented by the mean MDAS scores. Due to the MDAS cut off of more than 10 for the presence of delirium and an equal number of MDAS items, the prevalence of single symptoms was nearly 100% for all items. Thus a dichotomous variable with two levels was created, subjects with moderate and severe symptomatology being the first level and representing presence of delirium symptomatology, and subjects with absent to mild symptomatology being the second level representing the absence of symptomatology.

In a second step the dataset was defined representing a dichotomous variable with two levels: Hypoactive delirium and hyperactive delirium and performed the same analysis as for the entire delirium sample.

Due to the nature of the data representing an ordinal and categorical scale, Friedman's test for repeated measures was used for dependent measures, the Kruskal Wallis test for multiple measured of independent variables. For pair-wise comparison of independent samples, the Mann-Whitney U test was used; Pearson's Chi-square ($\chi 2$) - test was used for categorical variables. Exact tests were used when available.

# Results

The sample characteristics are given in Table 1.

We were able to retrieve 111 patients from our delirium database. The mean age of all patients was 65.6 years. Gender distribution was similar with 58.6% male and 41.4 % female patients. The study population was predominantly Caucasian (84%), but also included African-American (13%), Hispanic (2%), Asian (1%) and other ethnicity (1%). Cancer diagnoses were diverse with gastrointestinal cancer (23%), lung cancer (22%), brain cancer (11%), gynecological cancer (9%), sarcoma (7%), head and neck cancer (6%), and other malignancies (22%). Most patients had metastatic disease (48%), but also localized cancer (35%) and terminal cancer (17%). Brain metastases were present in 9%; 19% had a history of dementia. The delirium was multifactorial, most frequently encountered etiologies were the administration of opioids 88% and corticosteroids 47%, as well as hypoxia 37%, and infection 24%.

Delirium severity as measured by MDAS was 18.3. The KPS score was 24.1. Hypoactive delirium was present in 45% and hyperactive delirium in 55%.

## Phenomenology of delirium

Based on mean MDAS scores the most severe symptoms in delirium in descending order were impaired digit span (2.35), short term memory impairment (2.23), psychomotor abnormalities (2.14), disorientation (2.07), sleep-wake cycle disturbances (1.97), reduced ability to shift and maintain attention (1.96), disorganized thought (1.49) and disturbance of consciousness (1.96). The least severe symptoms were delusions (0.91) and perceptual disturbances (1.07) (Table 2).

Prevalence of moderate and severe symptoms (table 3): Psychomotor abnormality and impaired digit span were the most common symptoms with 95 and 90% presence respectively, followed in descending order by sleep-wake cycle disturbance and disturbance of consciousness (87% each), disorientation (78%), reduced ability to shift attention (71%), and disorganized thinking (40%). Perceptual disturbances and delusions were the least common symptoms with 37% and 32% respectively. Perceptual disturbances and delusions were not associated with cognitive impairment.

Sample characteristics of hypoactive and hyperactive delirium (Table 1)

Hypoactive and hyperactive delirium were present in 45% and 55%. The mean age of patients with hypoactive and hyperactive delirium was not significantly different: The mean age of patients with hypoactive delirium was 64.8 years, and in patients with hyperactive delirium the mean age was 66.2 years. There were no significant differences in gender distribution, history of dementia, cancer diagnoses, presence of brain metastases, nature and sum of etiologies. Terminal cancer was more often found in hypoactive delirium (26 and 10%).

**Table 1: Demographic and medical variables.** MDAS = Memorial Delirium Assessment Scale, KPS = Karnofsky Scale of Performance Status, MWU = Mann-Whitney U

| | All | Hypoactive | Hyperactive |
|---|---|---|---|
| Age | 65.6 (23-89, SD 13.6) | 64.8 (29-89, SD 12.5) | 66.2 (23-85, SD 14.6) |
| Previous dementia in % | 19 | 14 | 25 |
| Cancer diagnoses in % | | | |
| Gastroinstestinal | 23 | 28 | 20 |
| Lung | 22 | 20 | 23 |
| Brain | 11 | 6 | 15 |
| Gynecological | 9 | 10 | 8 |
| Sarcoma | 7 | 8 | 7 |
| Head and neck | 6 | 6 | 7 |
| other | 22 | 20 | 22 |
| Stage of cancer in %* | | | |
| Localized | 35 | 27 | 42 |
| Metastatic | 48 | 47 | 48 |
| Terminal | 17 | 27 | 10 |
| Etiologies (multifactorial) in % | | | |
| Opioids | 88 | 94 | 84 |
| Corticosteroids | 47 | 50 | 44 |
| Hypoxia | 37 | 42 | 33 |
| Infection | 24 | 30 | 20 |
| CNS disease | 13 | 14 | 12 |
| Dehydration | 5 | 8 | 3 |
| MDAS score** | 18.3 (11-30, SD 4.6) | 16.1 (11-25, SD 3.7) | 20.1 (12-30, SD 4.5) |
| KPS score | 24.1 (10-40, SD 5.8) | 23.4 (10-40, SD 6.3) | 24.6 (20-40, SD 5.3) |
| N | 111 | 50 | 61 |

*$\chi^2$=5.06; df=1; p<0.05
**MWU: 756.0; Z=-4.57; p<0.001

The total MDAS score was higher and delirium was overall more severe in hyperactive delirium than in hypoactive delirium (20.1 and 16.1). The level of functioning as measured by the KPS score was not significantly different between hypoactive and hyperactive delirium (23.4 and 24.6).

## Phenomenology of hypoactive and hyperactive delirium

Subjects with hyperactive delirium presented with more severe symptomatology than subjects with hypoactive delirium (Table 2). Differences existed in the cognitive domain, level of disorganization, perceptual disturbances, delusions and psychomotor abnormality. Disorientation was more severe in hyperactive delirium (2.21 and 1.90), short term memory impairment more pronounced (2.38 and 2.06), concentration more affected (impaired digit span 2.48 and 2.20), the attentional impairment was more severe (2.10 and 1.80), as were the level of disorganization (1.64 and 1.30), perceptual disturbances (1.56 and 0.54) and delusions (1.52 and 0.38), as well as psychomotor abnormality (2.23 and 2.04).

**Table 2: Delirium phenomenology: Mean MDAS scores. MDAS = Memorial Delirium Assessment Scale**

| Delirium phenomenology | All | Hypoactive | Hyperactive | Mann-Whitney U |
|---|---|---|---|---|
| 1 – Reduced consciousness | 1.94 (SD .43) | 1.94 (SD .47) | 1.93 (SD .40) | |
| 2 – Disorientation | 2.07 (SD .71) | 1.90 (SD .68) | 2.21 (SD .71) | 1164, Z=-2.33, p<0.05 |
| 3 – Short term memory impairment | 2.23 (SD .70) | 2.06 (SD .65) | 2.38 (SD .71) | 1133, Z=-2.53, p<0.05 |
| 4 – Impaired digit span | 2.35 (SD .66) | 2.20 (SD .67) | 2.48 (SD .62) | 1186, Z=-2.22, p<0.05 |
| 5 – Attentional impairment | 1.96 (SD .74) | 1.80 (SD .67) | 2.10 (SD .77) | 1196, Z=-2.01, p<0.05 |
| 6 – Disorganized thinking | 1.49 (SD .74) | 1.30 (SD .68) | 1.64 (SD .75) | 1138, Z=-2.59, p<0.05 |
| 7 – Perceptual disturbances | 1.10 (SD 1.09) | .54 (SD .76) | 1.56 (SD 1.10) | 748.5, Z=-4.83, p<0.001 |
| 8 – Delusions | 1.01 (SD 1.13) | .38 (SD .70) | 1.52 (SD 1.16) | 667, Z=-5.42, p<0.001 |
| 9 – Psychomotor abnormality | 2.14 (SD .48) | 2.04 (SD .45) | 2.23 (SD .50) | 1262, Z=-2.06, p<0.05 |
| 10 – Sleep-wake cycle disturbance | 1.97 (SD .51) | 1.90 (SD . 46) | 2.03 (SD .55) | |
| N | 111 | 50 | 61 | |

The prevalence of moderate and severe symptomatology (table 3) was increased in hyperactive delirium compared to hypoactive delirium. Disorganized thought process was present at 50.8% compared to 26% in hypoactive delirium, perceptual disturbances were significantly more often found in hyperactive delirium (57.4 and 12%), as were delusions with 47.5% over 12%. The prevalence of perceptual disturbances and delusions including mild symptomatology was 59.5% and 53.2% respectively.

# Discussion

We were able to show in this set of 111 delirium cases that delirium is a disorder of arousal disturbance, cognition and sleep-wake cycle disturbance. Cognitive ability was the most severely impaired domain, impaired digit span, a measure of attention and working memory, was the most affected cognitive task.

Our findings regarding the prevalence of arousal disturbance, disorientation, cognitive impairment, psychomotor behavior abnormality, and sleep-wake cycle disturbance compare to the findings in the review by Turkel et al.(2006) and in Cutting's study (1987) in respect to moderate and severe symptomatology, and show higher prevalence rates in respect to perceptual disturbances and delusions than Webster (2000).

Cognitive impairment was the most prominent feature in our sample. Impaired digit span was the most affected cognitive task, which is consistent with Meagher's findings. Similar to Meagher we were not able to find an association between cognitive impairment and perceptual disturbances as well as delusions (Meagher et al., 2007).

In a second step of this analysis we examined sample characteristics of subjects with hypoactive and hyperactive delirium and corresponding delirium phenomenology. We were not able to find differences between both subtypes of delirium in respect to age, gender distribution, history of dementia, cancer diagnoses, presence of brain metastases, nature and sum of etiologies. Etiologically delirium in cancer patients was multifactorial, and we were not able to find different etiologies contributing to either subtype of delirium We were able to find increased rates of terminal cancer in hypoactive delirium compared to hyperactive delirium suggesting that terminal cancer may more often result in hypoactive delirium. The level of functioning was not different between the motoric subtypes of delirium.

Overall delirium severity based on total MDAS scores was higher in hyperactive delirium, which in part may result in increased severities of disturbances in the cognitive domain, level of disorganization, perceptual disturbances and delusions, as well as psychomotor abnormality. This may also indicate that these symptoms are probably more severe in hyperactive delirium. In particular the prevalence of perceptual disturbances and delusions in hypoactive delirium, which has previously been reported to be as low as 3% by Ross (1991), and already indicated by Stagno to be as high as 51 and 43% (Stagno et al., 2004) was found to be more substantial. This analysis resulted in an overall prevalence of perceptual disturbances and delusions of 59.5% and 53.2% in hypoactive delirium respectively. It is important to recog-

**Table 3: Presence of moderate and severe delirium symptoms in percentages. MDAS = Memorial Delirium Assessment Scale**

| MDAS in % | All | Hypoactive | Hyperactive | Statistic |
|---|---|---|---|---|
| 1 – Reduced consciousness | 87.4 | 86 | 88.5 | |
| 2 – Disorientation | 78.4 | 72 | 83.6 | |
| 3 – Short term memory impairment | 84.7 | 82 | 86.9 | |
| 4 – Impaired digit span | 90.1 | 86 | 93.4 | |
| 5 –Attentional impairment | 71.2 | 66 | 75.4 | |
| 6 – Disorganized thinking | 39.6 | 26 | 50.8 | $\chi^2$7.07, df=1, p<0.05 |
| 7 – Perceptual disturbances | 36.9 | 12 | 57.4 | $\chi^2$24.29, df=1, p<0.001 |
| 8 – Delusions | 31.5 | 12 | 47.5 | $\chi^2$16.07, df=1, p<0.001 |
| 9 – Psychomotor abnormality | 94.6 | 92 | 96.7 | |
| 10 – Sleep-wake cycle disturbance | 87.4 | 84 | 90.2 | |
| N | 111 | 50 | 61 | |

nize that Ross' prevalences of perceptual disturbances and delusions in hypoactive delirium were based on the arousal disturbance subtyping approach, while Stagno's findings based the delirium subtypes on the MDAS and psychomotor abnormality.

Certain limitations have to be noted. The design of the study was cross-sectional, the evolution of symptoms over delirium severity cannot be reproduced. Longitudinal studies have suggested psychomotor abnormalities and sleep-wake cycle disturbances to be more often found in the early course of delirium (Fann et al., 2005) and disorientation, inattention, impaired memory and sleep disturbances to be more persistent symptoms throughout the course of delirium (Levkoff et al., 1994; McCusker et al., 2003). Within the sample of this study patients with cognitive deficits were not excluded. Brain metastases were present in 9%; 19% had a history of dementia. Delirium phenomenology has not been shown to be altered by the presence of dementia (Trzepacz et al., 1998). The etiology of delirium in our sample population of cancer patients was multifactorial and included medications with psychotropic effect. All subjects had cancer diagnoses and the generalizability of results to the non-cancer population remains to be studied.

Further studies are required to understand the effect of etiological factors on the presentation of delirium.

In summary, we were able to confirm the phenomenology of delirium as a disorder of arousal, cognition and sleep-wake cycle. Cognition was the most severely impaired domain, and concentration was the most affected cognitive task. Hyperactive delirium presented with more severe impairment in the cognitive domain, level of organization, perception and psychomotor behavior. Perceptual disturbances and delusions occur to a substantial rate in hypoactive delirium.

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