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TITLE PAGE

Title: Motor activity across delirium motor subtypes in geriatric patients assessed using body-worn sensors – a cross-sectional study

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ABSTRACT

Objectives: It remains unclear if geriatric patients with different delirium motor subtypes express different levels of motor activity. Thus, we used two accelerometer-based devices to simultaneously measure upright activity and wrist activity across delirium motor subtypes in a sample of geriatric patients.

Design: Cross-sectional study

Settings: Geriatric ward in a University Hospital

Participants: Sixty acutely admitted patients, ≥ 75 years, with DSM-5-delirium.

Outcome measures: Upright activity measured as upright time (minutes) and sit-to-stand transitions (numbers), total wrist activity (counts) and Wrist Activity in Sedentary position (WAS, % of sedentary time) during 24 hours on-going Delirium Motor Subtype Scale - subtyped delirium.

Results: Mean age was 86.7 years. We found no differences in upright time between the hyperactive (79.1 minutes), the hypoactive (37.8 minutes), and the mixed (50.1 minutes) groups (all $p > 0.28$), but more upright time for the no-subtype group (119.3 minutes) than the hypoactive group ($p=0.042$). For transitions, the no-subtype group had a higher number than both the hypoactive (54.3 vs 17.4 transitions, $p=0.005$) and the mixed group (54.3 vs 17.5 transitions, $p=0.013$). The hyperactive group had more total wrist activity than the hypoactive group (1.238×10^4 vs 586×10^4 counts, $p=0.009$). The hyperactive and the mixed groups had more WAS than the hypoactive group (20 % vs 11 %, $p=0.032$, and 19 % vs 11 %, $p=0.049$).

Conclusions: Patients with delirium demonstrated a low level of upright activity, with no differences between the hyperactive, hypoactive and mixed groups, possibly due to poor gait function in geriatric patients. However, the hyperactive and mixed groups had more WAS

than the hypoactive group, indicating true differences in motor activity across delirium motor subtypes, also in geriatric patients. Wrist activity appears more suitable than upright activity for both diagnostic purposes and activity monitoring in geriatric delirium.

ARTICLE SUMMARY

Strengths and limitations of the study

- We investigated motor activity across groups of hyperactive, hypoactive, mixed and no-subtype delirium in 60 acutely admitted geriatric patients with delirium.
- We diagnosed delirium according to the DSM-5 criteria and used the Delirium Motor Subtype Scale for motor subtyping
- By use of accelerometer data we evaluated motor disturbances in delirium as both upright activity, total wrist activity and wrist activity in a sedentary position
- The major strengths of the study are the use of the Delirium Motor Subtype Scale and the simultaneous use of data from two accelerometer-based devices
- The major limitations are the small number of patients in each group and the cross-sectional design

KEY WORDS: Delirium. Motor Subtypes. Geriatric. Actigraphy. Accelerometer.

INTRODUCTION

Delirium affects up to 50 % of hospitalized older patients[1] and is associated with increased risk of mortality, institutionalization and dementia[2]. The core symptoms of delirium are acute and/or fluctuating deficits in attention, alertness and cognition caused by physiological disturbances[3], and old age, comorbidity and cognitive and physical impairment are the most important risk factors[4]. Four motor subtypes of delirium have been identified – hyperactive, hypoactive, mixed and no-subtype delirium[5]. Most studies have found the highest mortality in patients with the hypoactive subtype[6-8].

Previous studies on delirium motor subtypes and prognosis have used different tools for subtyping, such as the Liptzin & Levkoff Schema[5], the Richmond Agitation and Sedation Scale[6] and the Memorial Delirium Assessment Scale[7, 9] with the two latter tools not specifically developed for motor subtyping. The concordance between subtyping tools is low[10], and it is therefore difficult to compare results from these studies[11] and draw firm conclusions about the prognosis of the different subtypes. Through systematic improvement of previous subtyping tools, Meagher et al. developed the Delirium Motor Subtype Scale (DMSS) which focuses on true motor features and no associated features like behavioral or psychiatric symptoms[12]. The DMSS lists four hyperactive and seven hypoactive features. Patients with two or more hyperactive features have hyperactive delirium, and patients with two or more hypoactive features have hypoactive delirium. Patients with both hyperactive and hypoactive features have mixed delirium, and those with fewer than two motor features have no-subtype delirium. DMSS is the only validated subtyping tool[13], including validation against objective measures of motor activity. Using a thigh-worn accelerometer-based device, Godfrey and Meagher studied 25 patients with DMSS-subtyped delirium in a palliative care unit. Patients with hyperactive delirium had higher amounts of motor activity than those with

hypoactive delirium, and patients with mixed delirium had amounts of motor activity between those of the hyperactive and the hypoactive groups[14].

To our knowledge, this is the only study comparing motor activity across delirium motor subtypes by use of accelerometer-based devices. The thigh-worn device used by Godfrey and Meagher uses the inclination of the thigh to distinguish between standing/stepping (upright) and sitting/lying (sedentary) positions[15], and since many older patients are not able to stand and/or walk due to frailty, amputations and sequels of stroke, this device might not capture all aspects of motor activity in geriatric patients. Still, there are reasons to believe that geriatric patients, independent of gait function, do express delirium motor disturbances. There is a need to investigate if there are differences in upright activity across DMSS-defined motor subtypes also in frail geriatric patients, furthermore to investigate if this patient group do express delirium motor disturbances in other ways than upright activity. The aim of this study is thus to compare motor activity across DMSS-defined delirium motor subtypes in hospitalized geriatric patients, using measures of 24-hour total wrist activity and wrist activity in a sedentary position, in addition to upright activity.

METHODS

Design, settings and participants

This is a cross-sectional study conducted at the geriatric ward at St. Olavs hospital, Trondheim, Norway, between May 6, 2015 and January 31, 2017. The ward has fifteen beds and is an integrated part of the medical department. The majority of patients are acutely admitted with medical conditions like infections, cardiorespiratory symptoms, cognitive symptoms or injuries after falls[16]. The patients receive comprehensive geriatric

assessment[17] and care by an interdisciplinary team of physicians, nurses, physiotherapists and occupational therapists.

The inclusion criteria were age ≥ 75 years, acute admittance to the geriatric ward and living in the city of Trondheim or three nearby municipalities. Patients transferred from other wards were eligible for inclusion if acutely admitted to the first ward. Staff nurses, physiotherapists or a physician included patients within 24 hours after admission.

Ethics

We collected written informed consent from the individual patients or from a proxy if the patient had obvious signs of cognitive impairment. We did not include cognitively impaired patients who refused participation. The Regional Committee for Medical and Health Research Ethics approved the study (REK Central 2015/474).

Diagnosis of delirium and motor subtypes

We diagnosed delirium according to the DSM-5 criteria[3], stressing that there had to be a somatic precipitating cause and that symptoms were not due to an existing dementia. We did delirium subtyping according to the DMSS and considered the motor subtype as stable during the 24-hour observation period[13]. We based the diagnoses on interviews with the patients, supplemented with information from proxies, nurses and chart reviews as described by Saczynski[18].

Activity Monitoring

We asked the patients to wear two body-worn accelerometer-based devices during their hospital stay; one activPAL (35×53×7 mm, 15 g, activPAL, PAL Technologies Ltd., Glasgow, United Kingdom) attached to the midpoint of the anterior right thigh using a waterproof tape and one ActiGraph GT3X (38x37x18 mm, 27 g, ActiGraph, Pensacola, FL,

USA) attached to the right wrist using a wristband. The member of staff responsible for inclusion immediately attached the devices and registered the time of attachment. Ward nurses removed the devices during CT and MRI-scans and showering, registering the time of removals and re-attachments. If the patient removed one or both devices more than once, the staff considered that the patient did not want to wear the devices and did not re-attach them. In this paper, we present data from patients who completed 24-hour activity monitoring with both devices centered on the time of diagnosis of delirium and motor subtype.

ActivPAL outcomes

The activPAL uses the inclination of the thigh to distinguish between upright and sedentary positions. Activity monitoring using activPAL devices is a validated method for quantifying physical activity in geriatric inpatients, except for measures of step count due to low gait speed[15]. We derived information regarding the duration of upright and sedentary events from the manufacturer's comma-separated values (CSV)-file using software version 7.3.32 (activPAL, PAL Technologies Ltd.) and a custom MATLAB (MATLAB version 7.1. The MathWorks Inc., Natick, MA, 2005) program to export an Excel spreadsheet (Office Excel version 11.0, Windows XP Professional, Microsoft, 2003) with outcome values for all patients. The minimum length of an upright event for the sample was 10 seconds. We used the activPAL Events file to determine the quantity and distribution of upright and sedentary events. We used upright time (minutes per 24 hours) and number of sit-to-stand transitions as measures of upright activity.

ActiGraph outcomes

The ActiGraph is a tri-axial accelerometer usually worn on the wrist or the hip[19, 20]. Using the ActiLife software (version 6.13.3), we filtered and accumulated the raw accelerometer signals into one-second non-overlapping epochs and exported them to CSV-files. We defined

a threshold of 0.5 (Units: ln (counts s^{-1})) to separate static from dynamic behavior of the wrist. We used the total number of counts above the threshold as outcome measure of total wrist activity.

Synchronized outcome

We synchronized both devices using their respective timestamps and exported the synchronized data from both devices into CSV-files. Based on time spent in a sedentary position, according to activPAL data, we generated a new variable indicating Wrist Activity in a Sedentary position (WAS). WAS describes the percentage of total sedentary time with wrist activity above the previously mentioned threshold.

Baseline characteristics

We collected demographic information on age, sex and nursing home stays from the patients' hospital records. We used the Short Physical Performance Battery[21] (SPPB, 0-12, 12 is the best score), completed as early as possible during the hospital stay, as a measure of physical function. An SPPB-score below 10 predicts all-cause mortality[22]. We retrospectively completed the Global Deterioration Scale[23] as a measure of pre-hospital cognitive impairment (GDS, 1-7, an increasing score indicates worse cognitive function) and the Barthel Index[24] as a measure of pre-hospital p-ADL-function (BI, 0-20, an increasing score indicates better p-ADL function). We calculated the APACHE II-score[25] (0-71, an increasing score indicates higher morbidity) and the Cumulative Illness Rating Scale[26] (CIRS, 0-56, a higher score indicates more serious chronic disease) as measures of morbidity and comorbidity.

Statistical analyses

We present descriptive statistics as means, standard deviations (SD) and ranges for continuous and ordinal variables and as percentages for dichotomous variables. We checked data for normality by visual inspection of Q-Q-plots and compared subgroups using ANOVA with Scheffé correction for normally distributed variables and Kruskal-Wallis'/ Mann-Whitney U test with Dunn correction for non-normally distributed variables. We considered two-sided p-values <0.05 as significant. We used SPSS version 24 for all statistical analyses.

Patients and public involvement

Neither patients nor public were involved in designing and conducting the study.

RESULTS

We enrolled 311 patients, of whom 103 (33.1 %) had delirium. The final analysis included 60 patients with complete data from both devices for a 24-hour period with on-going, motor subtyped, delirium. Among these, 15 had hyperactive, 20 hypoactive, 17 mixed and eight no-subtype delirium. Among those without complete activity monitoring, 10 had delirium only prior to arrival and could not be subtyped, 12 had hyperactive delirium, 10 had hypoactive delirium, seven had mixed delirium and four had no-subtype delirium. Figure 1 shows the flow of patients. As shown in Table 1, the 60 patients had a mean age of 86.7 years (SD 5.2) and a mean SPPB score of 2.7 (SD 3.1). Table 2 shows activity monitoring data for all groups and p-values for all pairwise comparisons. Figure 2 shows box-plots illustrating different aspects of motor activity across motor subtypes.

Table 1. Baseline characteristics for the entire sample and patients with hyperactive, hypoactive, mixed and no-subtype delirium.

	All	Hyper-active	Hypo-active	Mixed	No-subtype	p - value[1]
Number of patients	60	15	20	17	8	
Age (years), mean (SD)	86.7 (5.2)	86.3 (6.3)	85.5 (4.4)	88.7 (4.7)	86.1 (5.8)	0.28
p-ADL[2] Function Barthel Index (0-20), mean (SD)	15.5 (3.8)	16.3 (3.3)	14.2 (4.6)	15.8 (2.8)	16.5 (4.1)	0.29
Cognitive Function GDS[3] (1-7), mean (SD)	4.1 (1.3)	4.5 (1.5)	4.1 (1.1)	4.0 (1.4)	3.8 (1.0)	0.58
Physical Function SPPB[4] (0-12), mean (SD)	2.7 (3.1)	4.2 (3.8)	1.2 (1.5)	2.1 (2.9)	5.1 (3.0)	0.003
Number of drugs on admittance, mean (SD)	6.5 (3.2)	6.1 (4.0)	6.8 (2.8)	6.9 (3.5)	5.5 (2.3)	0.73
Acute Illness APACHE[5] II-score (0-71), mean (SD)	9.5 (2.8)	8.5 (1.9)	10.0 (3.6)	9.5 (2.5)	9.6 (2.4)	0.49
Comorbidity CIRS[6] (0-56), mean (SD)	15.2 (4.5)	14.6 (4.6)	16.0 (4.5)	14.9 (4.5)	14.8 (4.6)	0.81
Body Mass Index (kg/m^2) , mean (SD)	23.5 (3.6)	24.8 (2.3)	23.6 (3.8)	23.3 (3.9)	21.6 (4.5)	0.28
Female, n (%)	31(52)	8 (53)	8 (40)	10 (59)	5 (63)	0.61
Home living, n (%)	55 (92)	12 (80)	18 (90)	17 (100)	8 (100)	0.17
Dementia,[7] n (%)	43 (72)	10 (67)	15 (75)	13 (77)	5(63)	0.86

Footnotes: 1. P-values are calculated using one way ANOVA for continuous variables and Pearson's chi squared test for categorical variables. 2. Personal Activities of Daily Living. 3. Global Deterioration Scale. 4. Short Physical Performance Battery. 5. Acute Physiology and Chronic Health Evaluation. 6. Cumulative Illness Rating Scale. 7. Global Deterioration Scale ≥ 4

Table 2. Motor activity during 24 hours for the entire group and the four delirium motor subtypes, and pairwise comparisons of motor activity between delirium motor subtypes

Subtype		**Motor activity, mean (SD)**			
		Upright activity		Total wrist activity	Wrist activity in sedentary position
	N	Upright time (min)	Transitions (numbers)	Counts (numbers x 10^4)	WAS (% of time in sedentary position)
All	60	62.5 (68.2)	24.7 (21.3)	950 (588)	16.2 % (8.7 %)
Hyperactive	15	79.1 (65.0)	26.9 (19.9)	1238 (683)	19.7 % (9.0 %)
Hypoactive	20	37.8 (38.7)	17.4 (14.9)	586 (445)	11.2 % (7.6 %)
Mixed	17	50.1 (71.4)	17.5 (12.2)	1031 (531)	18.9 % (9.0 %)
No-subtype	8	119.3 (93.1)	54.3 (28.5)	1148 (433)	16.3 % (5.0 %)

Comparison	**p-values** [1,2]			
Hyperactive vs mixed	0.447	1.000	0.757	0.995
Hyperactive vs hypoactive	0.281	0.835	0.009	0.032
Mixed vs hypoactive	1.000	1.000	0.109	0.049
No subtype vs hypoactive	0.042	0.005	0.111	0.520
No subtype vs hyperactive	1.000	0.247	0.986	0.826
No subtype vs mixed	0.070	0.013	0.967	0.906

Footnotes: 1. Pairwise comparisons for upright activity are Dunn – corrected. 2. Pairwise comparisons for wrist activity are Scheffé – corrected.

Upright activity

Upright time and transitions were not normally distributed due to low levels of upright activity. The Kruskal-Wallis test showed significant differences between the groups for both upright time ($p = 0.015$) and transitions ($p = 0.005$). There were no significant differences between the hyperactive, hypoactive and mixed groups. We found however, a significantly higher amount of upright time in the no-subtype group than in the hypoactive group (mean 119.3 min vs 37.8 min, $p = 0.042$) and a significantly higher number of transitions in the no-subtype group than in both the hypoactive and mixed groups (mean no-subtype 54.3 vs hypoactive 17.4, $p = 0.005$, and mixed 17.5, $p = 0.013$).

Total wrist activity

ANOVA analysis showed significant overall group differences for total number of counts ($p = 0.004$). We found a significant difference between the hyperactive and the hypoactive group, with a significantly higher number of counts (1238×10^4 vs 586×10^4, $p = 0.009$) in the hyperactive group.

Wrist activity in sedentary position

ANOVA analysis showed significant overall group differences for WAS ($p = 0.011$). Comparing the hyperactive and the hypoactive group, we found a significantly higher amount of WAS (20 % vs 11 %, $p = 0.032$) in the hyperactive group. Comparing the mixed group and the hypoactive group, we found a significantly higher amount of WAS (19 % vs 11 %, $p = 0.049$) in the mixed group.

DISCUSSION

In this cross-sectional study on hospitalized geriatric patients with delirium, we found a low level of upright activity with no significant differences between the hyperactive, hypoactive and mixed groups. However, the no-subtype group had significantly more upright time than the hypoactive group and a significantly higher number of transitions than both the hypoactive and the mixed groups. In addition, we found significant differences in WAS between the hyperactive, hypoactive and the mixed groups, with higher amounts of WAS in the hyperactive and mixed groups than in the hypoactive group.

To our knowledge, this is the first study to simultaneously measure motor activity as both upright activity and wrist activity in geriatric patients with delirium motor subtyped by use of the DMSS, the only validated tool for motor subtyping. Godfrey conducted the only previous study analyzing motor activity across DMSS-defined motor subtypes, but reported only upright activity[14]. Patients included were substantially younger than our sample (mean age 70.7 years vs 86.7 years), and the overall finding was significant differences between the hyperactive and the hypoactive groups with the mixed group between the other groups. We could not reproduce these findings, probably because our patients are frail with heavily impaired gait function illustrated by a mean SPPB-score of 2.7, and on a group level are incapable of expressing hyperactivity through increased amounts of upright activity. For total wrist activity, however, our results complies with Godfrey's with a significant difference between the hyperactive and the hypoactive groups and the mixed group between these. In our material WAS separates the hypoactive group from both the hyperactive and mixed groups, which complies with the DMSS that states that both the hyperactive and the mixed groups have some sort of hyperactivity. In sum, the results from wrist actigraphy illustrates that also geriatric patients with delirium have motor disturbances that that applies with the DMSS and can be captured by use of devices measuring aspects of motor activity other than upright time,

and that wrist activity, especially during sedentary behavior, is a promising motor activity measure in frail, geriatric patients since it is independent of the patient's gait function.

Figure 2 illustrates a large spread within all groups for all measures of motor activity. This probably reflects that factors other than motor subtype also influence motor activity in geriatric patients with delirium, such as the nature of the acute disease, frailty, subcortical brain pathology like Parkinson's disease and vascular dementia, lower limb function and sequels after strokes and amputations. In our sample, this is illustrated with the low overall level of physical function measured by SPPB with the highest, but still low, scores in the hyperactive and the no-subtype group, indicating that geriatric patients with delirium are hardly able to get out of bed and walk. When it comes to activity monitoring data, the 25% of the patients with hyperactive delirium had low levels of upright activity with a mean value of 79 minutes of upright time and 27 transitions per 24 hours. This indicates that geriatric patients with delirium, and even with hyperactive delirium, spend a majority of time in a sedentary position. Thus clinicians cannot rely on wandering and changing of posture when looking for delirium. Our results indicate that patients with both hyperactive and mixed delirium express hyperactivity through wrist activity, and that clinicians should evaluate signs of restlessness in bed or in a chair rather than judging upright activity when looking for delirium.

This is the first study to report results of an accelerometer-based motor activity analysis in the no-subtype group. Some speculate that the no-subtype group represents less serious, questionable or resolving delirium[13, 27]. In our study, the main finding for this group was a higher amount of upright activity than both the hypoactive and mixed groups. The no-subtype group spent 119.3 minutes out of 24 hours in upright position, which is almost identical to the 117.1 minutes of a general case-mix of hospitalized geriatric patients that we have recently reported from our ward[16]. This might indicate that the three motor subtypes hyperactive,

hypoactive and mixed delirium represent fundamental motor disturbances eventually resulting in reduced motor activity, whereas the no-subtype represents a milder delirium not reaching the threshold for developing motor disturbances and thereby have a higher level of motor activity, more similar to patients without delirium. Thus, the important differences in motor activity in patients with delirium may be between the majority with motor symptoms and the minority without motor symptoms. This view is supported by a study finding that 38 patients with un-subtyped delirium had less wrist activity than 32 patients without delirium during the first 24 hours after cardiac surgery[28]. In sum, the results from studies using activity monitoring in patients with delirium indicate that delirium, in general, is associated with less, and not more motor activity, and also raise the question if the term "hyperactive delirium" is misleading.

Strengths and limitations

The major strengths of this study are the simultaneous use of two accelerometer-based devices to measure both upright activity and wrist activity simultaneously, and the use of DMSS for motor subtyping. This is also the first study to include the no-subtype group in analyses of motor activity. Our patients are old and frail. This is a strength since such patients frequently have delirium and were not recruited in previous research on delirium and activity monitoring, but also means that our results are not necessarily applicable to patients with delirium in other settings. The sample of 60 patients is large compared to the only previous study in the field, although the small number of patients in each subgroup is the major limitation, creating a risk of type II error. There is also a possibility that patients with the most intense delirium were not included or did not complete activity monitoring, introducing a possible inclusion bias influencing the results. Another important limitation is the cross-sectional design. A recent publication indicates that a substantial number of patients with delirium fluctuate between subtypes[27], but we believe this has limited impact on our results

since the activity monitoring was done in a limited time-frame centered on the time of diagnosing and subtyping.

Conclusions

In this sample of frail, geriatric patients with delirium, we found a low level of upright activity with no differences between the hyperactive, hypoactive and mixed groups for neither upright time nor transitions. However, we found differences across these groups in both total wrist activity and WAS, indicating that there are true differences in motor activity across DMSS-defined motor subtypes also in geriatric patients with delirium. Our results indicate that restlessness while in a sedentary position is a more reliable clinical feature than wandering and changing of posture when looking for delirium in geriatric patients. Further research should address how motor features can improve the diagnostic work-up of delirium in general and explore possible therapeutic consequences for the different delirium motor subtypes.

FIGURE LEGENDS

Figure 1. Flow chart summarizing reasons why patients did not complete 24-hour activity monitoring.

Figure 2. Box-plots with delirium motor subtypes on the x-axes and time in upright position, sit-to-stand transitions, counts and Wrist Activity in Sedentary position (WAS) in percent of total time in sedentary position on the y-axes. The horizontal line in each box is the median, and the bottom and top of the boxes are the quartiles.

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The material presented in this article was presented as an eight minute lecture at the European Delirium Association yearly meeting in 2017.

STATEMENTS

Author Contributorship

SE did the initial drafting of the article, had the main responsibility for data collection and for diagnosing and subtyping delirium

AKB processed and analysed the activity monitoring data

OS is the project manager and designed the study. He also participated in diagnosing and subtyping of delirium.

SL had the main responsibility for the statistical analyses

IS participated in designing and planning the study with particular responsibility in data collection at the geriatric ward.

TBW participated in designing and planning the study with particular responsibility in the diagnostic work-up of delirium and subtyping.

KT participated in designing and planning the study, with a particular responsibility in planning data collection with the accelerometer-based devices.

All authors have critically read and approved the final manuscript

Competing interests

Alan Kevin Bourke worked at NTNU, Department of Neuromedicine and Movement Sciences, when completing his contribution to this article. After finishing his contribution, but before the article was submitted, he started working at Roche Pharmaceutical Research and Early Development (pRED), Roche Innovation Center Basel, F.Hoffmann-La Roche Ltt, 124 Grenzacherstrasse, Basel, CH 4070, Switzerland.

The other authors have no competing interests to report.

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Other statements

Data Sharing: Datasets from this study are not available since we do not have the consent to share the data neither from The Regional Committee for Medical and Health Research Ethics nor from the patients.

Patient consent: We confirm that all patients or a proxy consented for participation based on the concept of written informed consent.

Ethical approval: The Regional Committee for Medical and Health Research Ethics of Mid-Norway approved the study (REK Central 2015/474).

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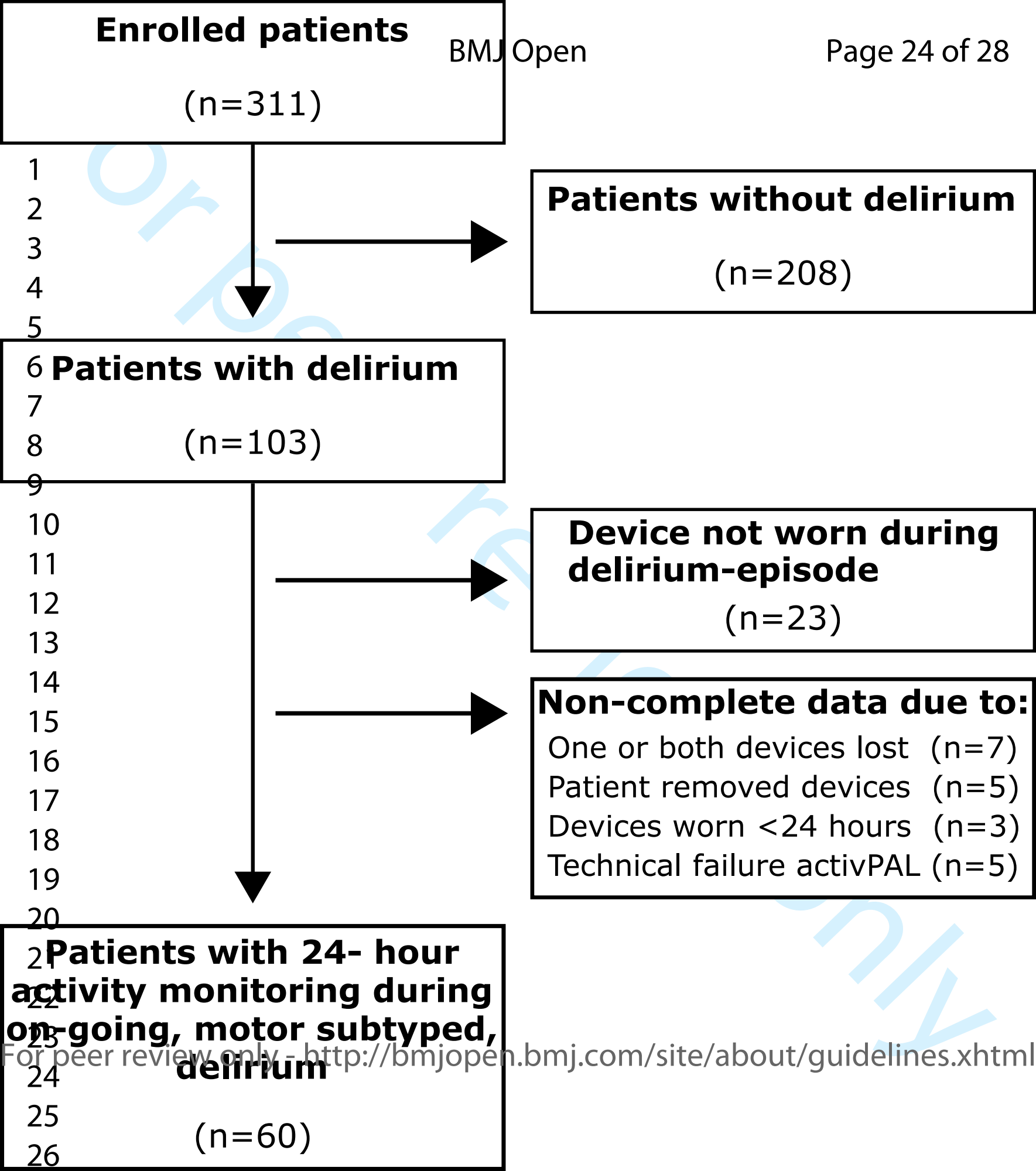
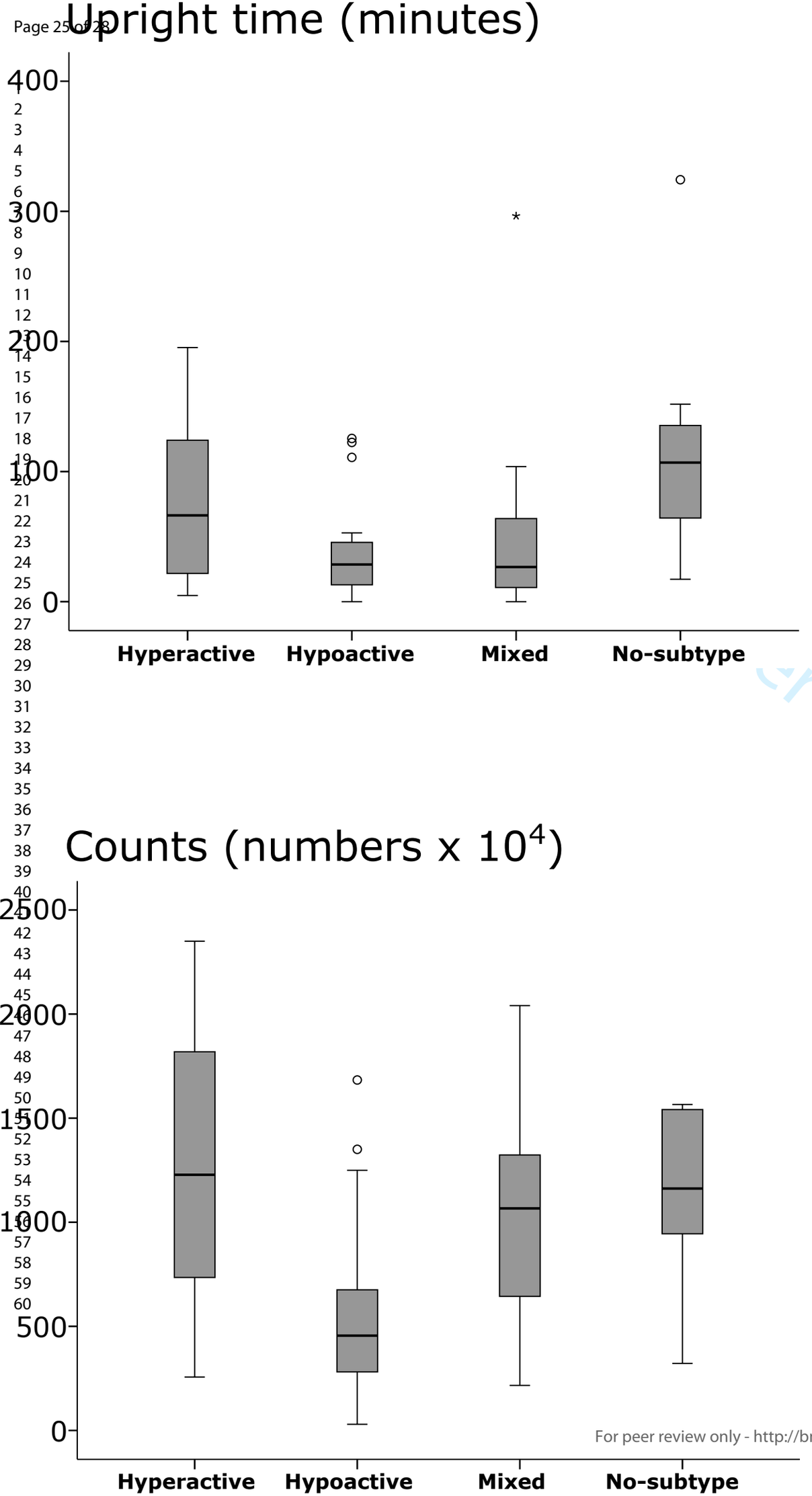
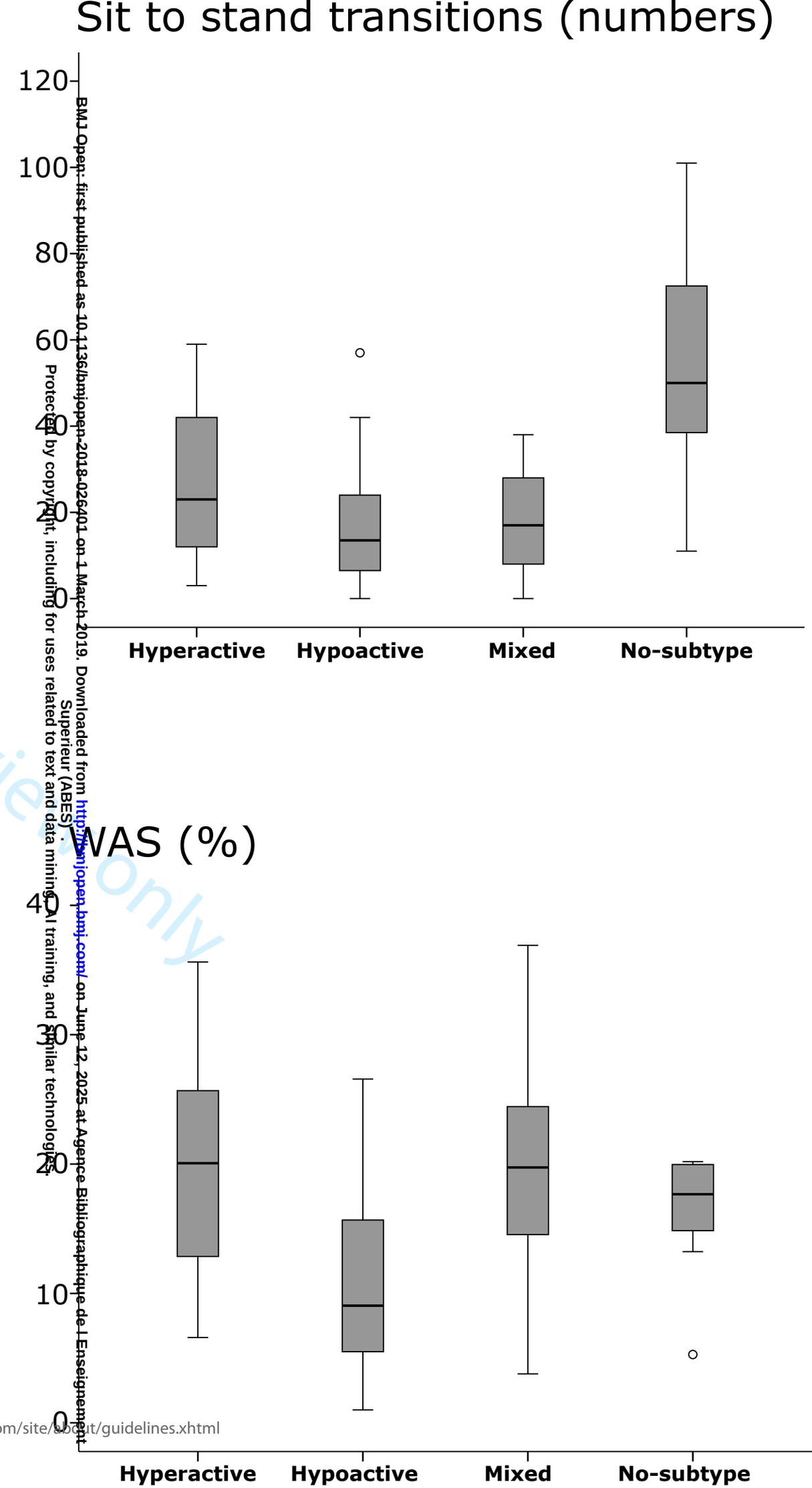
Delirium and motor activity







Reporting checklist for cross sectional study.

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		Reporting Item	Page Number
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	#3	State specific objectives, including any prespecified hypotheses	5
Study design	#4	Present key elements of study design early in the paper	5
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants.	6

	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	6-9
Bias	#9	Describe any efforts to address potential sources of bias	15
Study size	#10	Explain how the study size was arrived at	9
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	9, 45
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	9
	#12b	Describe any methods used to examine subgroups and interactions	9
	#12c	Explain how missing data were addressed	9
	#12d	If applicable, describe analytical methods taking account of sampling strategy	Not relevant
	#12e	Describe any sensitivity analyses	Not relevant
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	9, Fig1
	#13b	Give reasons for non-participation at each stage	9, Fig1
	#13c	Consider use of a flow diagram	Fig 1
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and	Table 1

		unexposed groups if applicable.	
	#14b	Indicate number of participants with missing data for each variable of interest	9, Fig1
Outcome data	#15	Report numbers of outcome events or summary measures. Give information separately for exposed and unexposed groups if applicable.	9, table 2
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12, table 2
	#16b	Report category boundaries when continuous variables were categorized	Not relevant
	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	9, table 2
Key results	#18	Summarise key results with reference to study objectives	13
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	15
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	13-15
Generalisability	#21	Discuss the generalisability (external validity) of the study results	13-16
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

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Motor activity across delirium motor subtypes in geriatric patients assessed using body-worn sensors – a cross-sectional study

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TITLE PAGE

Title: Motor activity across delirium motor subtypes in geriatric patients assessed using body-worn sensors – a cross-sectional study

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ABSTRACT

Objectives: It remains unclear if geriatric patients with different delirium motor subtypes express different levels of motor activity. Thus, we used two accelerometer-based devices to simultaneously measure upright activity and wrist activity across delirium motor subtypes in geriatric patients.

Design: Cross-sectional study

Settings: Geriatric ward in a University Hospital

Participants: Sixty acutely admitted patients, ≥ 75 years, with DSM-5-delirium.

Outcome measures: Upright activity measured as upright time (minutes) and sit-to-stand transitions (numbers), total wrist activity (counts) and Wrist Activity in Sedentary position (WAS, % of sedentary time) during 24 hours on-going Delirium Motor Subtype Scale - subtyped delirium.

Results: Mean age was 86.7 years. Fifteen had hyperactive, 20 hypoactive, 17 mixed and eight had no-subtype delirium. We found more upright time in the no-subtype group than in the hypoactive group (119.3 vs 37.8 minutes, p=0.042), but no differences between the hyperactive, the hypoactive and the mixed groups (79.1 vs 37.8 vs 50.1 minutes, all p's>0.28). The no-subtype group had a higher number of transitions than the hypoactive (54.3 vs 17.4, p=0.005) and the mixed groups (54.3 vs 17.5, p=0.013). The hyperactive group had more total wrist activity than the hypoactive group (1.238 x 10^4 vs 586 x 10^4 counts, p=0.009). The hyperactive and the mixed groups had more WAS than the hypoactive group (20 % vs 11 %, p=0.032, and 19 % vs 11 %, p=0.049).

Conclusions: Geriatric patients with delirium demonstrated a low level of upright activity, with no differences between the hyperactive, hypoactive and mixed groups, possibly due to

poor gait function. The hyperactive and mixed groups had more WAS than the hypoactive group, indicating true differences in motor activity across delirium motor subtypes, also in geriatric patients. Wrist activity appears more suitable than upright activity for both diagnostic purposes and activity monitoring in geriatric delirium.

ARTICLE SUMMARY

Strengths and limitations of the study

- We investigated motor activity across groups of hyperactive, hypoactive, mixed and no-subtype delirium in 60 acutely admitted geriatric patients with delirium.
- We diagnosed delirium according to the DSM-5 criteria and used the Delirium Motor Subtype Scale for motor subtyping
- By use of accelerometer data we evaluated motor disturbances in delirium as both upright activity, total wrist activity and wrist activity in a sedentary position
- The major strengths of the study are the use of the Delirium Motor Subtype Scale and the simultaneous use of data from two accelerometer-based devices
- The major limitations are the small number of patients in each group and the cross-sectional design

KEY WORDS: Delirium. Motor Subtypes. Geriatric. Actigraphy. Accelerometer.

INTRODUCTION

Delirium affects up to 50 % of hospitalized older patients[1] and is associated with increased risk of mortality, institutionalization and dementia[2]. The core symptoms of delirium are acute and/or fluctuating deficits in attention, alertness and cognition that are physiological consequences of an underlying medical condition[3], and old age, comorbidity and cognitive and physical impairment are the most important risk factors[4]. Four motor subtypes of delirium have been identified – hyperactive, hypoactive, mixed and no-subtype delirium[5]. Most studies have found the highest mortality in patients with the hypoactive subtype[6-8].

Previous studies on delirium motor subtypes and prognosis have used different tools for subtyping, such as the Liptzin & Levkoff Schema[5], the Richmond Agitation and Sedation Scale[6] and the Memorial Delirium Assessment Scale[7, 9] with the two latter tools not specifically developed for motor subtyping. The concordance between subtyping tools is low[10], and it is therefore difficult to compare results from these studies[11] and draw firm conclusions about the prognosis of the different subtypes. Through systematic improvement of previous subtyping tools, Meagher et al. developed the Delirium Motor Subtype Scale (DMSS) which focuses on true motor features and no associated features like behavioral or psychiatric symptoms[12]. The DMSS lists four hyperactive and seven hypoactive features. Patients with two or more hyperactive features have hyperactive delirium, and patients with two or more hypoactive features have hypoactive delirium. Patients with both hyperactive and hypoactive features have mixed delirium, and those with fewer than two motor features have no-subtype delirium. DMSS is the only validated subtyping tool[13], including validation against objective measures of motor activity. Using a thigh-worn accelerometer-based device, Godfrey and Meagher studied 25 patients with DMSS-subtyped delirium in a palliative care unit. Patients with hyperactive delirium had higher amounts of motor activity than those with

hypoactive delirium, and patients with mixed delirium had amounts of motor activity between those of the hyperactive and the hypoactive groups[14].

To our knowledge, this is the only study comparing motor activity across delirium motor subtypes by use of accelerometer-based devices. The thigh-worn device used by Godfrey and Meagher uses the inclination of the thigh to distinguish between standing/stepping (upright) and sitting/lying (sedentary) positions[15], and since many older patients are not able to stand and/or walk due to frailty, amputations and sequels of stroke, this device might not capture all aspects of motor activity in geriatric patients. Still, there are reasons to believe that geriatric patients, independent of gait function, do express delirium motor disturbances. There is a need to investigate if there are differences in upright activity across DMSS-defined motor subtypes also in frail geriatric patients, furthermore to investigate if this patient group do express delirium motor disturbances in other ways than upright activity. The aim of this study is thus to compare motor activity across DMSS-defined delirium motor subtypes in hospitalized geriatric patients, using midnight to midnight recordings of total wrist activity and wrist activity in a sedentary position, in addition to upright activity.

METHODS

Design, settings and participants

This is a cross-sectional study investigating motor activity by use of accelerometer-based devices in a limited time-frame in a selected group of geriatric patients with verified, motor subtyped and on-going delirium. The study was conducted at the geriatric ward at St. Olavs hospital, Trondheim, Norway, between May 6, 2015 and January 31, 2017. The ward has fifteen beds and is an integrated part of the medical department. The majority of patients are acutely admitted with medical conditions like infections, cardiorespiratory symptoms,

cognitive symptoms or injuries after falls[16]. The patients receive comprehensive geriatric assessment[17] and care by an interdisciplinary team of physicians, nurses, physiotherapists and occupational therapists. The ward has only single bed rooms and is built to enhance orientation and physical activity. There is no use of physical restraints.

The inclusion criteria were age ≥ 75 years and acute admittance to the geriatric ward. We did not exclude any patients due to diagnosis like dementia, prevalent delirium, other neuropsychiatric conditions or sensory deficits. Patients transferred from other wards were eligible for inclusion if acutely admitted to the first ward. Staff members included patients as soon as possible and always within 24 hours after admission. Only patients with complete 24-hour activity monitoring centered on the time of diagnosis of delirium were included in the final analysis.

Ethics

We collected written informed consent from the individual patients or from a proxy if the patient had obvious signs of cognitive impairment. We did not include cognitively impaired patients who refused participation. The Regional Committee for Medical and Health Research Ethics approved the study (REK Central 2015/474).

Diagnosis of delirium and motor subtypes

Two geriatricians (SE and OS) who had received supervision by an experienced delirium researcher (TBW), diagnosed delirium according to the DSM-5 criteria[3], stressing that there had to be a somatic precipitating cause. To diagnose delirium superimposed on dementia we interviewed nurses and proxies and reviewed medical records to clarify that the present symptoms were not due to an existing dementia. We did delirium subtyping according to the DMSS and considered the motor subtype as stable during the observation period[13]. We based the diagnoses on interviews with the patients, supplemented with information from

proxies, nurses and chart reviews as described by Saczynski[18] and used all available information from the chosen 24-hour period of activity monitoring when deciding motor subtypes.

Activity monitoring

We asked the patients to wear two body-worn accelerometer-based devices during their hospital stay; one activPAL (35×53×7 mm, 15 g, activPAL, PAL Technologies Ltd., Glasgow, United Kingdom) attached to the midpoint of the anterior right thigh using a waterproof tape and one ActiGraph GT3X (38x37x18 mm, 27 g, ActiGraph, Pensacola, FL, USA) attached to the right wrist using a wristband. A nurse or a physiotherapist not participating in diagnosing and subtyping of delirium attached the devices immediately after inclusion and registered the time of attachment, making sure the devices did not interfere with equipment for monitoring and intravenous lines. Ward nurses removed the devices during CT and MRI-scans and showering, registering the time of removals and re-attachments. If the patient removed one or both devices more than once, the staff considered that the patient did not want to wear the devices and did not re-attach them. Patients wore the devices until discharge. A Data Scientist not involved in any other parts of the project (AKB), analyzed the activity data when the recruitment of patients was terminated. Consequently, the assessors of DMSS (SE, OS) were blinded to the results of activity monitoring.

ActivPAL outcomes

The activPAL uses the inclination of the thigh to distinguish between upright and sedentary positions. Activity monitoring using activPAL devices is a validated method for quantifying physical activity in geriatric inpatients, except for measures of step count due to low gait speed[15]. We derived information regarding the duration of upright and sedentary events from the manufacturer's comma-separated values (CSV)-file using software version 7.3.32

(activPAL, PAL Technologies Ltd.) and a custom MATLAB (MATLAB version 7.1. The MathWorks Inc., Natick, MA, 2005) program to export an Excel spreadsheet (Office Excel version 11.0, Windows XP Professional, Microsoft, 2003) with outcome values for all patients. The minimum length of an upright event for the sample was 10 seconds. We used the activPAL Events file to determine the quantity and distribution of upright and sedentary events. We used upright time (minutes per 24 hours) and total number of sit-to-stand transitions as measures of upright activity.

ActiGraph outcomes

The ActiGraph is a tri-axial accelerometer usually worn on the wrist or the hip[19, 20]. Using the ActiLife software (version 6.13.3), we filtered and accumulated the raw accelerometer signals into one-second non-overlapping epochs and exported them to CSV-files. We defined a threshold of 0.5 (Units: ln (counts s^{-1})) to separate static from dynamic behavior of the wrist. We used the total number of counts above the threshold as outcome measure of total wrist activity.

Synchronized outcome

We synchronized both devices using their respective timestamps and exported the synchronized data from both devices into CSV-files. Based on time spent in a sedentary position, according to activPAL data, we generated a new variable indicating Wrist Activity in a Sedentary position (WAS). WAS describes the percentage of total sedentary time with wrist activity above the previously mentioned threshold.

Baseline characteristics

We collected demographic information on age, sex and nursing home stays from the patients' hospital records. We used the Short Physical Performance Battery[21] (SPPB, 0-12, 12 is the best score), completed as early as possible during the hospital stay, as a measure of physical function. An SPPB score below 10 predicts all-cause mortality[22]. We retrospectively completed the Global Deterioration Scale[23] as a measure of pre-hospital cognitive impairment (GDS, 1-7, an increasing score indicates worse cognitive function) and the Barthel Index[24] as a measure of pre-hospital p-ADL-function (BI, 0-20, an increasing score indicates better p-ADL function). We calculated the APACHE II-score[25] (0-71, an increasing score indicates higher morbidity) and the Cumulative Illness Rating Scale[26] (CIRS, 0-56, a higher score indicates more serious chronic disease) as measures of morbidity and comorbidity.

Statistical analyses

We present descriptive statistics as means, standard deviations (SD) and ranges for continuous and ordinal variables and as percentages for dichotomous variables. We checked data for normality by visual inspection of Q-Q-plots and compared subgroups using ANOVA with Scheffé correction for normally distributed variables and Kruskal-Wallis'/ Mann-Whitney U test with Dunn correction for non-normally distributed variables. We considered two-sided p-values <0.05 as significant. We used SPSS version 24 for all statistical analyses and report the results according to the STROBE cross sectional reporting guidelines.

Patients and public involvement

Neither patients nor public were directly involved in the development of the research questions, study design, outcome measures, recruitment and conduct of the study. A summary of the main results will be communicated to the study participants on request.

RESULTS

We enrolled 311 patients, of whom 103 (33.1 %) had delirium. The final analysis included 60 patients with complete data from both devices for a 24-hour period with on-going, motor subtyped, delirium. Among these, 15 had hyperactive, 20 hypoactive, 17 mixed and eight no-subtype delirium. Among those without complete activity monitoring, 10 had delirium only prior to arrival and could not be subtyped, 12 had hyperactive delirium, 10 had hypoactive delirium, seven had mixed delirium and four had no-subtype delirium. Figure 1 shows the flow of patients. As shown in Table 1, the 60 patients had a mean age of 86.7 years (SD 5.2) and a mean SPPB score of 2.7 (SD 3.1). Table 2 shows activity monitoring data for all groups and p-values for all pairwise comparisons. Figure 2 shows box-plots illustrating different aspects of motor activity across motor subtypes.

Table 1. Baseline characteristics for patients with hyperactive, hypoactive, mixed and no-subtype delirium.

	Hyperactive (n=15)	**Hypoactive (n=20)**	**Mixed (n=17)**	**No-subtype (n=8)**	p - value[1]
	Mean (Standard Deviations)				
Age (years)	86.3 (6.3)	85.5 (4.4)	88.7 (4.7)	86.1 (5.8)	0.28
p-ADL[2] Function Barthel Index score (0-20)	16.3 (3.3)	14.2 (4.6)	15.8 (2.8)	16.5 (4.1)	0.29
Cognitive Function GDS[3] score (1-7)	4.5 (1.5)	4.1(1.1)	4.0 (1.4)	3.8 (1.0)	0.58
Physical Function SPPB[4] score (0-12)	4.2 (3.8)	1.2 (1.5)	2.1 (2.9)	5.1(3.0)	0.003
Drugs on admittance (no)	6.1(4.0)	6.8 (2.8)	6.9 (3.5)	5.5 (2.3)	0.73
Acute Illness APACHE[5] II score (0-71)	8.5 (1.9)	10.0 (3.6)	9.5 (2.5)	9.6 (2.4)	0.49
Comorbidity CIRS[6] score (0-56)	14.6 (4.6)	16.0 (4.5)	14.9 (4.5)	14.8 (4.6)	0.81
Body Mass Index (kg/m²)	24.8 (2.3)	23.6 (3.8)	23.3 (3.9)	21.6 (4.5)	0.28
	Number (%)				
Female (%)	8 (53)	8 (40)	10 (59)	5 (63)	0.61
Living at home (%)	12 (80)	18 (90)	17 (100)	8 (100)	0.17
Dementia[7] (%)	10 (67)	15 (75)	13 (77)	5 (63)	0.86

Footnotes: 1. P-values are calculated using one way ANOVA for continuous variables and Pearson's chi squared test for categorical variables. 2. Personal Activities of Daily Living. 3. Global Deterioration Scale. 4. Short Physical Performance Battery. 5. Acute Physiology and Chronic Health Evaluation. 6. Cumulative Illness Rating Scale. 7. Global Deterioration Scale ≥ 4

Table 2. Motor activity during 24 hours for the entire group and the four delirium motor subtypes, and pairwise comparisons of motor activity between delirium motor subtypes

Subtype		**Motor activity, mean (SD)**			
		Upright activity		Total wrist activity	Wrist activity in sedentary position
	N	Upright time (min)	Transitions (numbers)	Counts (numbers x 10^4)	WAS (% of time in sedentary position)
All	60	62.5 (68.2)	24.7 (21.3)	950 (588)	16.2 % (8.7 %)
Hyperactive	15	79.1 (65.0)	26.9 (19.9)	1238 (683)	19.7 % (9.0 %)
Hypoactive	20	37.8 (38.7)	17.4 (14.9)	586 (445)	11.2 % (7.6 %)
Mixed	17	50.1 (71.4)	17.5 (12.2)	1031 (531)	18.9 % (9.0 %)
No-subtype	8	119.3 (93.1)	54.3 (28.5)	1148 (433)	16.3 % (5.0 %)
Comparison				**p-values** [1,2]	
Hyperactive vs mixed		0.447	1.000	0.757	0.995
Hyperactive vs hypoactive		0.281	0.835	0.009	0.032
Mixed vs hypoactive		1.000	1.000	0.109	0.049
No subtype vs hypoactive		0.042	0.005	0.111	0.520
No subtype vs hyperactive		1.000	0.247	0.986	0.826
No subtype vs mixed		0.070	0.013	0.967	0.906

Footnotes: 1. Pairwise comparisons for upright activity are Dunn – corrected. 2. Pairwise comparisons for wrist activity are Scheffé – corrected.

Upright activity

Upright time and transitions were not normally distributed due to low levels of upright activity. The Kruskal-Wallis test showed significant differences between the groups for both upright time ($p = 0.015$) and transitions ($p = 0.005$). There were no significant differences between the hyperactive, hypoactive and mixed groups. We found however, a significantly higher amount of upright time in the no-subtype group than in the hypoactive group (mean 119.3 min vs 37.8 min, $p = 0.042$) and a significantly higher number of transitions in the no-subtype group than in both the hypoactive and mixed groups (mean no-subtype 54.3 vs hypoactive 17.4, $p = 0.005$, and mixed 17.5, $p = 0.013$).

Total wrist activity

ANOVA analysis showed significant overall group differences for total number of counts ($p = 0.004$). We found a significant difference between the hyperactive and the hypoactive group, with a significantly higher number of counts (1238×10^4 vs 586×10^4, $p = 0.009$) in the hyperactive group.

Wrist activity in sedentary position

ANOVA analysis showed significant overall group differences for WAS ($p = 0.011$). Comparing the hyperactive and the hypoactive group, we found a significantly higher amount of WAS (20 % vs 11 %, $p = 0.032$) in the hyperactive group. Comparing the mixed group and the hypoactive group, we found a significantly higher amount of WAS (19 % vs 11 %, $p = 0.049$) in the mixed group.

DISCUSSION

In this cross-sectional study on hospitalized geriatric patients with delirium, we found a low level of upright activity with no significant differences between the hyperactive, hypoactive and mixed groups. However, the no-subtype group had significantly more upright time than the hypoactive group and a significantly higher number of transitions than both the hypoactive and the mixed groups. In addition, we found significant differences in WAS between the hyperactive, hypoactive and the mixed groups, with higher amounts of WAS in the hyperactive and mixed groups than in the hypoactive group.

To our knowledge, this is the first study to simultaneously measure motor activity as both upright activity and wrist activity in geriatric patients with delirium motor subtyped by use of the DMSS, the only validated tool for motor subtyping. Godfrey conducted the only previous study analyzing motor activity across DMSS-defined motor subtypes, but reported only upright activity[14]. Patients included were substantially younger than our sample (mean age 70.7 years vs 86.7 years), and the overall finding was significant differences between the hyperactive and the hypoactive groups with the mixed group between the other groups. We could not reproduce these findings, probably because our patients are frail with heavily impaired gait function illustrated by a mean SPPB score of 2.7, and on a group level are incapable of expressing hyperactivity through increased amounts of upright activity. For total wrist activity, however, our results complies with Godfrey's with a significant difference between the hyperactive and the hypoactive groups and the mixed group between these. In our material WAS separates the hypoactive group from both the hyperactive and mixed groups, which complies with the DMSS that states that both the hyperactive and the mixed groups have some sort of hyperactivity. In sum, the results from wrist actigraphy illustrates that also geriatric patients with delirium have motor disturbances that applies with the DMSS and can be captured by use of devices measuring aspects of motor activity other than upright time, and

that wrist activity, especially during sedentary behavior, is a promising motor activity measure in frail, geriatric patients since it is independent of the patient's gait function.

Figure 2 illustrates a large variability within all groups for all measures of motor activity. This probably reflects that factors other than motor subtype also influence motor activity in geriatric patients with delirium, such as acute disease, frailty, brain pathology like Parkinson's disease and vascular dementia, lower limb function and sequels after strokes and amputations. We identified discharge diagnosis with the potential of influencing motor activity in a negative way like strokes, fractures and difficulties to walk due to frailty or subcortical brain pathology in 33 out of 60 patients. In our sample, a low level of physical function is illustrated by low SBBP score in all groups, illustrating that geriatric patients with delirium are hardly able to get out of bed and walk. According to SPPB score, the hyperactive and the no-subtype groups seem to have better physical function, but this might reflect the impact of the motor subtype on the SPPB performance rather than patients' physical function at baseline. When it comes to activity monitoring data, the patients with hyperactive delirium had low levels of upright activity, with a mean value of 79 minutes of upright time and 27 transitions per 24 hours. This illustrates that geriatric patients with delirium, and even those with hyperactive delirium, spend a majority of time in a sedentary position. Thus, clinicians cannot rely on wandering and changing of posture when looking for delirium. Our results indicate that patients with both hyperactive and mixed delirium express hyperactivity through wrist activity, and that clinicians should evaluate signs of restlessness in bed or in a chair rather than judging upright activity when looking for delirium.

This is the first study to report results of an accelerometer-based motor activity analysis in the no-subtype group. Some speculate that the no-subtype group represents less serious, questionable or resolving delirium[13, 27]. In our study, the main finding for this group was a higher amount of upright activity than both the hypoactive and mixed groups. The no-subtype

group spent 119.3 minutes out of 24 hours in upright position, which is almost identical to the 117.1 minutes of a general case-mix of hospitalized geriatric patients that we have recently reported from our ward[16]. This might indicate that the three motor subtypes hyperactive, hypoactive and mixed delirium represent fundamental motor disturbances eventually resulting in reduced motor activity, whereas the no-subtype represents a milder delirium not reaching the threshold for developing motor disturbances and thereby have a higher level of motor activity, more similar to patients without delirium. Thus, the important differences in motor activity in patients with delirium may be between the majority with motor symptoms and the minority without motor symptoms. This view is supported by a study finding that 38 patients with un-subtyped delirium had less wrist activity than 32 patients without delirium during the first 24 hours after cardiac surgery[28]. In sum, the results from studies using activity monitoring in patients with delirium indicate that delirium, in general, is associated with less, and not more motor activity, and also raise the question if the term "hyperactive delirium" is misleading.

Strengths and limitations

The major strengths of this study are the simultaneous use of two accelerometer-based devices to measure both upright activity and wrist activity simultaneously, and the use of DMSS for motor subtyping. This is also the first study to include the no-subtype group in analyses of motor activity. Our patients are old and frail. This is a strength since such patients frequently have delirium and were not recruited in previous research on delirium and activity monitoring, but also a limitation since our results are not necessarily applicable to patients with delirium in other settings. The sample of 60 patients is large compared to the only previous study in the field, although the small number of patients in each subgroup is the major limitation, creating a risk of type II error and preventing firm conclusions. There is also a possibility that patients with the most intense delirium were not included or did not

complete activity monitoring, introducing a possible inclusion bias influencing the results. A potential bias is that patients with hyperactive delirium were slightly overrepresented among those who did not complete 24-hour activity monitoring. Another important limitation is the cross-sectional design. A recent publication indicates that a substantial number of patients with delirium fluctuate between subtypes[27], but we believe this has limited impact on our results since the activity monitoring was done in a limited time-frame centered on the time of diagnosing and subtyping.

Conclusions

In this sample of frail, geriatric patients with delirium, we found a low level of upright activity with no differences between the hyperactive, hypoactive and mixed groups for neither upright time nor transitions. However, we found differences across these groups in both total wrist activity and WAS, indicating that there are true differences in motor activity across DMSS-defined motor subtypes also in geriatric patients with delirium. Our results indicate that restlessness while in a sedentary position is a more reliable clinical feature than wandering and changing of posture when looking for delirium in geriatric patients. Further research should address how motor features can improve the diagnostic work-up of delirium in general and explore possible therapeutic consequences for the different delirium motor subtypes.

FIGURE LEGENDS

Figure 1. Flow chart summarizing reasons why patients did not complete 24-hour activity monitoring.

Figure 2. Box-plots with delirium motor subtypes on the x-axes and time in upright position, sit-to-stand transitions, counts and Wrist Activity in Sedentary position (WAS) in percent of total time in sedentary position on the y-axes. The horizontal line in each box is the median, and the bottom and top of the boxes are the quartiles.

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The material presented in this article was presented as an eight-minute lecture at the European Delirium Association yearly meeting in 2017.

STATEMENTS

Author Contributorship

SE did the initial drafting of the article, had the main responsibility for data collection and for diagnosing and subtyping delirium

AKB processed and analysed the activity monitoring data

OS is the project manager and designed the study. He also participated in diagnosing and subtyping of delirium.

SL had the main responsibility for the statistical analyses

IS participated in designing and planning the study with particular responsibility in data collection at the geriatric ward.

TBW participated in designing and planning the study with particular responsibility in the diagnostic work-up of delirium and subtyping.

KT participated in designing and planning the study, with a particular responsibility in planning data collection with the accelerometer-based devices.

All authors have critically read and approved the final manuscript

Competing interests

Alan Kevin Bourke worked at NTNU, Department of Neuromedicine and Movement Sciences, when completing his contribution to this article. After finishing his contribution, but before the article was submitted, he started working at Roche Pharmaceutical Research and Early Development (pRED), Roche Innovation Center Basel, F.Hoffmann-La Roche Ltt, 124 Grenzacherstrasse, Basel, CH 4070, Switzerland.

The other authors have no competing interests to report.

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Other statements

Data Sharing: Datasets from this study are not available since we do not have the consent to share the data neither from The Regional Committee for Medical and Health Research Ethics nor from the patients.

Patient consent: We confirm that all patients or a proxy consented for participation based on the concept of written informed consent.

Ethical approval: The Regional Committee for Medical and Health Research Ethics of Mid-Norway approved the study (REK Central 2015/474).

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Delirium and motor activity

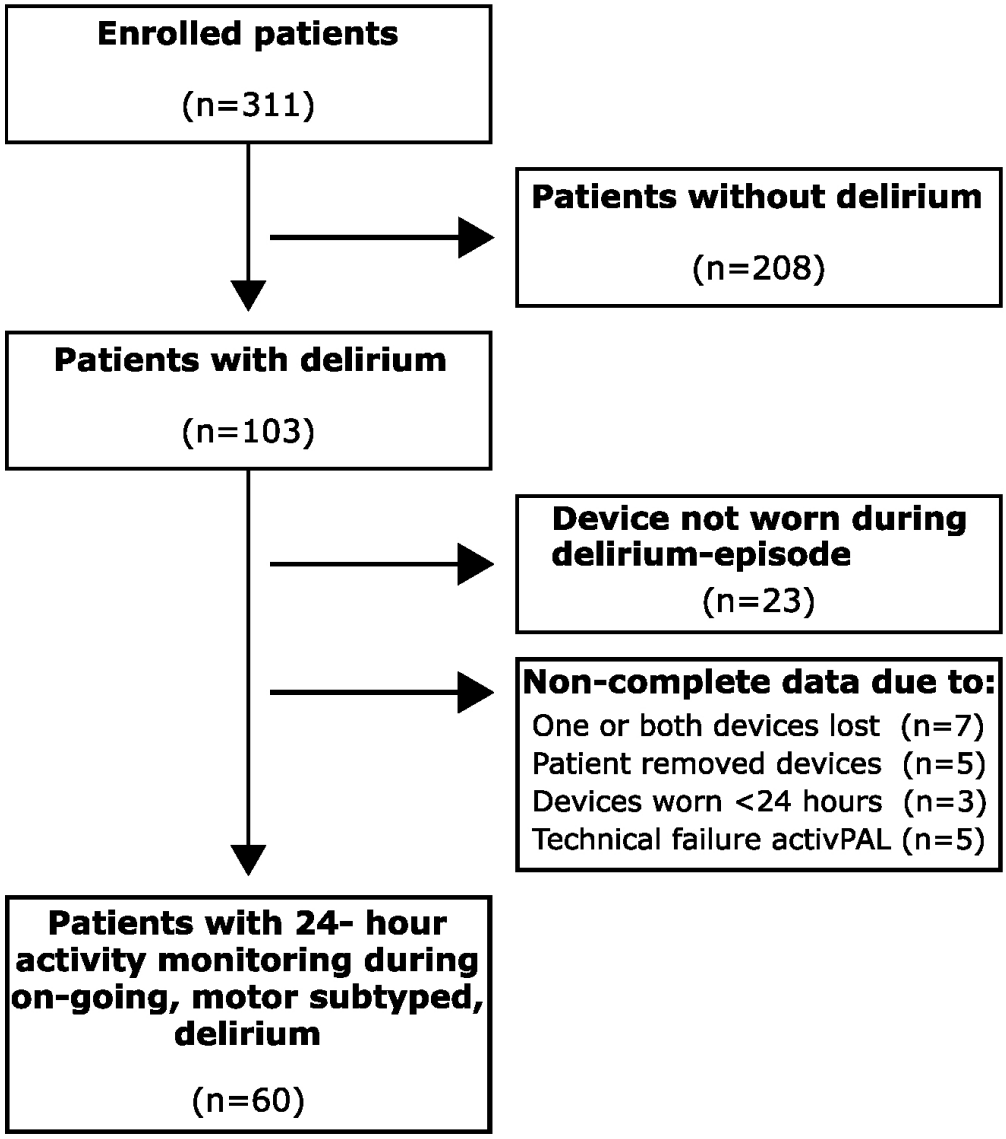

Figure 1. Flow chart summarizing reasons why patients did not complete 24-hour activity monitoring.

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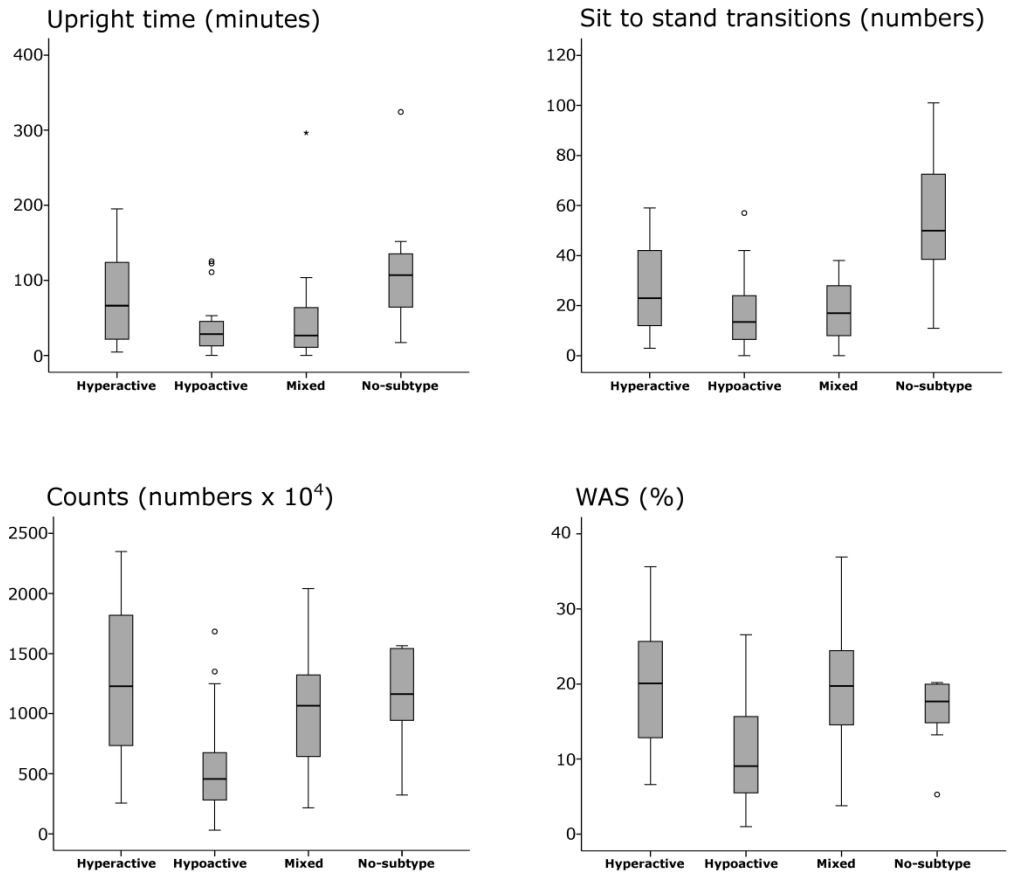

Figure 2. Box-plots with delirium motor subtypes on the x-axes and time in upright position, sit-to-stand transitions, counts and Wrist Activity in Sedentary position (WAS) in percent of total time in sedentary position on the y-axes. The horizontal line in each box is the median, and the bottom and top of the boxes are the quartiles.

356x308mm (300 x 300 DPI)

Reporting checklist for cross sectional study.

Based on the STROBE cross sectional guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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In your methods section, say that you used the STROBE cross sectional reporting guidelines, and cite them as:

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		Reporting Item	Page Number
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	#3	State specific objectives, including any prespecified hypotheses	5
Study design	#4	Present key elements of study design early in the paper	5
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants.	6

	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	6-9
Bias	#9	Describe any efforts to address potential sources of bias	15
Study size	#10	Explain how the study size was arrived at	9
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	9, 45
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	9
	#12b	Describe any methods used to examine subgroups and interactions	9
	#12c	Explain how missing data were addressed	9
	#12d	If applicable, describe analytical methods taking account of sampling strategy	Not relevant
	#12e	Describe any sensitivity analyses	Not relevant
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	9, Fig1
	#13b	Give reasons for non-participation at each stage	9, Fig1
	#13c	Consider use of a flow diagram	Fig 1
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and	Table 1

		unexposed groups if applicable.	
	#14b	Indicate number of participants with missing data for each variable of interest	9, Fig1
Outcome data	#15	Report numbers of outcome events or summary measures. Give information separately for exposed and unexposed groups if applicable.	9, table 2
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12, table 2
	#16b	Report category boundaries when continuous variables were categorized	Not relevant
	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	9, table 2
Key results	#18	Summarise key results with reference to study objectives	13
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	15
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	13-15
Generalisability	#21	Discuss the generalisability (external validity) of the study results	13-16
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

BMJ Open

Motor activity across delirium motor subtypes in geriatric patients assessed using body-worn sensors – a Norwegian cross-sectional study

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TITLE PAGE

Title: Motor activity across delirium motor subtypes in geriatric patients assessed using body-worn sensors – a Norwegian cross-sectional study

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ABSTRACT

Objectives: It remains unclear if geriatric patients with different delirium motor subtypes express different levels of motor activity. Thus, we used two accelerometer-based devices to simultaneously measure upright activity and wrist activity across delirium motor subtypes in geriatric patients.

Design: Cross-sectional study

Settings: Geriatric ward in a university hospital in Norway

Participants: Sixty acutely admitted patients, ≥ 75 years, with DSM-5-delirium.

Outcome measures: Upright activity measured as upright time (minutes) and sit-to-stand transitions (numbers), total wrist activity (counts) and Wrist Activity in Sedentary position (WAS, % of sedentary time) during 24 hours on-going Delirium Motor Subtype Scale - subtyped delirium.

Results: Mean age was 86.7 years. Fifteen had hyperactive, 20 hypoactive, 17 mixed and eight had no-subtype delirium. We found more upright time in the no-subtype group than in the hypoactive group (119.3 vs 37.8 minutes, p=0.042), but no differences between the hyperactive, the hypoactive and the mixed groups (79.1 vs 37.8 vs 50.1 minutes, all p's>0.28). The no-subtype group had a higher number of transitions than the hypoactive (54.3 vs 17.4, p=0.005) and the mixed groups (54.3 vs 17.5, p=0.013). The hyperactive group had more total wrist activity than the hypoactive group (1.238 x 10^4 vs 586 x 10^4 counts, p=0.009). The hyperactive and the mixed groups had more WAS than the hypoactive group (20 % vs 11 %, p=0.032, and 19 % vs 11 %, p=0.049).

Conclusions: Geriatric patients with delirium demonstrated a low level of upright activity, with no differences between the hyperactive, hypoactive and mixed groups, possibly due to

poor gait function. The hyperactive and mixed groups had more WAS than the hypoactive group, indicating true differences in motor activity across delirium motor subtypes, also in geriatric patients. Wrist activity appears more suitable than upright activity for both diagnostic purposes and activity monitoring in geriatric delirium.

ARTICLE SUMMARY

Strengths and limitations of the study

- We investigated motor activity across groups of hyperactive, hypoactive, mixed and no-subtype delirium in 60 acutely admitted geriatric patients with delirium
- We diagnosed delirium according to the DSM-5 criteria and used the Delirium Motor Subtype Scale for motor subtyping
- By use of accelerometer data we evaluated motor disturbances in delirium as both upright activity, total wrist activity and wrist activity in a sedentary position
- The major strengths of the study are the use of the Delirium Motor Subtype Scale and the simultaneous use of data from two accelerometer-based devices
- The major limitations are the small number of patients in each group and the cross-sectional design

KEY WORDS: Delirium. Motor Subtypes. Geriatric. Actigraphy. Accelerometer.

INTRODUCTION

Delirium affects up to 50 % of hospitalized older patients[1] and is associated with increased risk of mortality, institutionalization and dementia[2]. The core symptoms of delirium are acute and/or fluctuating deficits in attention, alertness and cognition that are physiological consequences of an underlying medical condition[3], and old age, comorbidity and cognitive and physical impairment are the most important risk factors[4]. Four motor subtypes of delirium have been identified – hyperactive, hypoactive, mixed and no-subtype delirium[5]. Most studies have found the highest mortality in patients with the hypoactive subtype[6-8].

Previous studies on delirium motor subtypes and prognosis have used different tools for subtyping, such as the Liptzin & Levkoff Schema[5], the Richmond Agitation and Sedation Scale[6] and the Memorial Delirium Assessment Scale[7, 9] with the two latter tools not specifically developed for motor subtyping. The concordance between subtyping tools is low[10], and it is therefore difficult to compare results from these studies[11] and draw firm conclusions about the prognosis of the different subtypes. Through systematic improvement of previous subtyping tools, Meagher et al. developed the Delirium Motor Subtype Scale (DMSS) which focuses on true motor features and no associated features like behavioral or psychiatric symptoms[12]. The DMSS lists four hyperactive and seven hypoactive features. Patients with two or more hyperactive features have hyperactive delirium, and patients with two or more hypoactive features have hypoactive delirium. Patients with both hyperactive and hypoactive features have mixed delirium, and those with fewer than two motor features have no-subtype delirium. DMSS is the only validated subtyping tool[13], including validation against objective measures of motor activity. Using a thigh-worn accelerometer-based device, Godfrey and Meagher studied 25 patients with DMSS-subtyped delirium in a palliative care unit. Patients with hyperactive delirium had higher amounts of motor activity than those with

hypoactive delirium, and patients with mixed delirium had amounts of motor activity between those of the hyperactive and the hypoactive groups[14].

To our knowledge, this is the only study comparing motor activity across delirium motor subtypes by use of accelerometer-based devices. The thigh-worn device used by Godfrey and Meagher uses the inclination of the thigh to distinguish between standing/stepping (upright) and sitting/lying (sedentary) positions[15], and since many older patients are not able to stand and/or walk due to frailty, amputations and sequels after stroke, this device might not capture all aspects of motor activity in geriatric patients. Still, there are reasons to believe that geriatric patients, independent of gait function, do express delirium motor disturbances. There is a need to investigate if there are differences in upright activity across DMSS-defined motor subtypes also in frail geriatric patients, furthermore to investigate if this patient group do express delirium motor disturbances in other ways than upright activity. The aim of this study is thus to compare motor activity across DMSS-defined delirium motor subtypes in hospitalized geriatric patients, using midnight to midnight recordings of total wrist activity and wrist activity in a sedentary position, in addition to upright activity.

METHODS

Design, settings and participants

This is a cross-sectional study investigating motor activity by use of accelerometer-based devices in a limited time-frame in a selected group of geriatric patients with verified, motor subtyped and on-going delirium. The study was conducted at the geriatric ward at St. Olavs hospital, Trondheim, Norway, between May 6, 2015 and January 31, 2017. The ward has fifteen beds and is an integrated part of the medical department. The majority of patients are acutely admitted with medical conditions like infections, cardiorespiratory symptoms,

cognitive symptoms or injuries after falls[16]. The patients receive comprehensive geriatric assessment[17] and care by an interdisciplinary team of physicians, nurses, physiotherapists and occupational therapists. The ward has only single bed rooms and is built to enhance orientation and physical activity. There is no use of physical restraints.

The inclusion criteria were age ≥ 75 years and acute admittance to the geriatric ward. We did not exclude any patients due to diagnosis like dementia, prevalent delirium, other neuropsychiatric conditions or sensory deficits. Patients transferred from other wards were eligible for inclusion if acutely admitted to the first ward. Staff members included patients as soon as possible and always within 24 hours after admission. Only patients with complete 24-hour activity monitoring centered on the time of diagnosis of delirium were included in the final analysis.

Ethics

We collected written informed consent from the individual patients or from a proxy if the patient had obvious signs of cognitive impairment. We did not include cognitively impaired patients who refused participation. The Regional Committee for Medical and Health Research Ethics approved the study (REK Central 2015/474).

Diagnosis of delirium and motor subtypes

Two geriatricians (SE and OS) who had received supervision by an experienced delirium researcher (TBW), diagnosed delirium according to the DSM-5 criteria[3], stressing that there had to be a somatic precipitating cause. To diagnose delirium superimposed on dementia we interviewed nurses and proxies and reviewed medical records to clarify that the present symptoms were not due to an existing dementia. We did delirium subtyping according to the DMSS and considered the motor subtype as stable during the observation period[13]. We based the diagnoses on interviews with the patients, supplemented with information from

proxies, nurses and chart reviews as described by Saczynski[18] and used all available information from the chosen 24-hour period of activity monitoring when deciding motor subtypes.

Activity monitoring

We asked the patients to wear two body-worn accelerometer-based devices during their hospital stay; one activPAL (35×53×7 mm, 15 g, activPAL, PAL Technologies Ltd., Glasgow, United Kingdom) attached to the midpoint of the anterior right thigh using a waterproof tape and one ActiGraph GT3X (38x37x18 mm, 27 g, ActiGraph, Pensacola, FL, USA) attached to the right wrist using a wristband. A nurse or a physiotherapist not participating in diagnosing and subtyping of delirium attached the devices immediately after inclusion and registered the time of attachment, making sure the devices did not interfere with equipment for monitoring and intravenous lines. Ward nurses removed the devices during CT and MRI-scans and showering, registering the time of removals and re-attachments. If the patient removed one or both devices more than once, the staff considered that the patient did not want to wear the devices and did not re-attach them. Patients wore the devices until discharge. A Data Scientist not involved in any other parts of the project (AKB), analyzed the activity data when the recruitment of patients was terminated. Consequently, the assessors of DMSS (SE, OS) were blinded to the results of activity monitoring.

ActivPAL outcomes

The activPAL uses the inclination of the thigh to distinguish between upright and sedentary positions. Activity monitoring using activPAL devices is a validated method for quantifying physical activity in geriatric inpatients, except for measures of step count due to low gait speed[15]. We derived information regarding the duration of upright and sedentary events from the manufacturer's comma-separated values (CSV)-file using software version 7.3.32

(activPAL, PAL Technologies Ltd.) and a custom MATLAB (MATLAB version 7.1. The MathWorks Inc., Natick, MA, 2005) program to export an Excel spreadsheet (Office Excel version 11.0, Windows XP Professional, Microsoft, 2003) with outcome values for all patients. The minimum length of an upright event for the sample was 10 seconds. We used the activPAL Events file to determine the quantity and distribution of upright and sedentary events. We used upright time (minutes per 24 hours) and total number of sit-to-stand transitions as measures of upright activity.

ActiGraph outcomes

The ActiGraph is a tri-axial accelerometer usually worn on the wrist or the hip[19, 20]. Using the ActiLife software (version 6.13.3), we filtered and accumulated the raw accelerometer signals into one-second non-overlapping epochs and exported them to CSV-files. We defined a threshold of 0.5 (Units: ln (counts s^{-1})) to separate static from dynamic behavior of the wrist. We used the total number of counts above the threshold as outcome measure of total wrist activity.

Synchronized outcome

We synchronized both devices using their respective timestamps and exported the synchronized data from both devices into CSV-files. Based on time spent in a sedentary position, according to activPAL data, we generated a new variable indicating Wrist Activity in a Sedentary position (WAS). WAS describes the percentage of total sedentary time with wrist activity above the previously mentioned threshold.

Baseline characteristics

We collected demographic information on age, sex and nursing home stays from the patients' hospital records. We used the Short Physical Performance Battery[21] (SPPB, 0-12, 12 is the best score), completed as early as possible during the hospital stay, as a measure of physical function. An SPPB score below 10 predicts all-cause mortality[22]. We retrospectively completed the Global Deterioration Scale[23] as a measure of pre-hospital cognitive impairment (GDS, 1-7, an increasing score indicates worse cognitive function) and the Barthel Index[24] as a measure of pre-hospital p-ADL-function (BI, 0-20, an increasing score indicates better p-ADL function). We calculated the APACHE II-score[25] (0-71, an increasing score indicates higher morbidity) and the Cumulative Illness Rating Scale[26] (CIRS, 0-56, a higher score indicates more serious chronic disease) as measures of morbidity and comorbidity.

Statistical analysis

We present descriptive statistics as means, standard deviations (SD) and ranges for continuous and ordinal variables and as percentages for dichotomous variables. We checked data for normality by visual inspection of Q-Q-plots and compared subgroups using ANOVA with Scheffé correction for normally distributed variables and Kruskal-Wallis'/ Mann-Whitney U test with Dunn correction for non-normally distributed variables. We considered two-sided p-values <0.05 as significant. We used SPSS version 24 for all statistical analyses and report the results according to the STROBE cross sectional reporting guidelines.

Patients and public involvement

Neither patients nor public were directly involved in the development of the research questions, study design, outcome measures, recruitment and conduct of the study. A summary of the main results will be communicated to the study participants on request.

RESULTS

We enrolled 311 patients, of whom 103 (33.1 %) had delirium. The final analysis included 60 patients with complete data from both devices for a 24-hour period with on-going, motor subtyped, delirium. Among these, 15 had hyperactive, 20 hypoactive, 17 mixed and eight no-subtype delirium. Among those without complete activity monitoring, 10 had delirium only prior to arrival and could not be subtyped, 12 had hyperactive delirium, 10 had hypoactive delirium, seven had mixed delirium and four had no-subtype delirium. Figure 1 shows the flow of patients. As shown in Table 1, the 60 patients had a mean age of 86.7 years (SD 5.2) and a mean SPPB score of 2.7 (SD 3.1). Table 2 shows activity monitoring data for all groups and p-values for all pairwise comparisons. Figure 2 shows box-plots illustrating different aspects of motor activity across motor subtypes.

Table 1. Baseline characteristics for patients with hyperactive, hypoactive, mixed and no-subtype delirium.

	Hyperactive (n=15)	**Hypoactive (n=20)**	**Mixed (n=17)**	**No-subtype (n=8)**	p - value[1]
	Mean (Standard Deviations)				
Age (years)	86.3 (6.3)	85.5 (4.4)	88.7 (4.7)	86.1 (5.8)	0.28
p-ADL[2] Function Barthel Index score (0-20)	16.3 (3.3)	14.2 (4.6)	15.8 (2.8)	16.5 (4.1)	0.29
Cognitive Function GDS[3] score (1-7)	4.5 (1.5)	4.1(1.1)	4.0 (1.4)	3.8 (1.0)	0.58
Physical Function SPPB[4] score (0-12)	4.2 (3.8)	1.2 (1.5)	2.1 (2.9)	5.1(3.0)	0.003
Drugs on admittance (no)	6.1(4.0)	6.8 (2.8)	6.9 (3.5)	5.5 (2.3)	0.73
Acute Illness APACHE[5] II score (0-71)	8.5 (1.9)	10.0 (3.6)	9.5 (2.5)	9.6 (2.4)	0.49
Comorbidity CIRS[6] score (0-56)	14.6 (4.6)	16.0 (4.5)	14.9 (4.5)	14.8 (4.6)	0.81
Body Mass Index (kg/m²)	24.8 (2.3)	23.6 (3.8)	23.3 (3.9)	21.6 (4.5)	0.28
	Number (%)				
Female (%)	8 (53)	8 (40)	10 (59)	5 (63)	0.61
Living at home (%)	12 (80)	18 (90)	17 (100)	8 (100)	0.17
Dementia[7] (%)	10 (67)	15 (75)	13 (77)	5 (63)	0.86

Footnotes: 1. P-values are calculated using one way ANOVA for continuous variables and Pearson's chi squared test for categorical variables. 2. Personal Activities of Daily Living. 3. Global Deterioration Scale. 4. Short Physical Performance Battery. 5. Acute Physiology and Chronic Health Evaluation. 6. Cumulative Illness Rating Scale. 7. Global Deterioration Scale ≥ 4

Table 2. Motor activity during 24 hours for the entire group and the four delirium motor subtypes, and pairwise comparisons of motor activity between delirium motor subtypes

Subtype		**Motor activity, mean (SD)**			
		Upright activity		Total wrist activity	Wrist activity in sedentary position
	N	Upright time (min)	Transitions (numbers)	Counts (numbers x 10^4)	WAS (% of time in sedentary position)
All	60	62.5 (68.2)	24.7 (21.3)	950 (588)	16.2 % (8.7 %)
Hyperactive	15	79.1 (65.0)	26.9 (19.9)	1238 (683)	19.7 % (9.0 %)
Hypoactive	20	37.8 (38.7)	17.4 (14.9)	586 (445)	11.2 % (7.6 %)
Mixed	17	50.1 (71.4)	17.5 (12.2)	1031 (531)	18.9 % (9.0 %)
No-subtype	8	119.3 (93.1)	54.3 (28.5)	1148 (433)	16.3 % (5.0 %)
Comparison				**p-values** [1,2]	
Hyperactive vs mixed		0.447	1.000	0.757	0.995
Hyperactive vs hypoactive		0.281	0.835	0.009	0.032
Mixed vs hypoactive		1.000	1.000	0.109	0.049
No subtype vs hypoactive		0.042	0.005	0.111	0.520
No subtype vs hyperactive		1.000	0.247	0.986	0.826
No subtype vs mixed		0.070	0.013	0.967	0.906

Footnotes: 1. Pairwise comparisons for upright activity are Dunn – corrected. 2. Pairwise comparisons for wrist activity are Scheffé – corrected.

Upright activity

Upright time and transitions were not normally distributed due to low levels of upright activity. The Kruskal-Wallis test showed significant differences between the groups for both upright time ($p = 0.015$) and transitions ($p = 0.005$). There were no significant differences between the hyperactive, hypoactive and mixed groups. We found however, a significantly higher amount of upright time in the no-subtype group than in the hypoactive group (mean 119.3 min vs 37.8 min, $p = 0.042$) and a significantly higher number of transitions in the no-subtype group than in both the hypoactive and mixed groups (mean no-subtype 54.3 vs hypoactive 17.4, $p = 0.005$, and mixed 17.5, $p = 0.013$).

Total wrist activity

ANOVA analysis showed significant overall group differences for total number of counts ($p = 0.004$). We found a significant difference between the hyperactive and the hypoactive group, with a significantly higher number of counts (1238×10^4 vs 586×10^4, $p = 0.009$) in the hyperactive group.

Wrist activity in sedentary position

ANOVA analysis showed significant overall group differences for WAS ($p = 0.011$). Comparing the hyperactive and the hypoactive group, we found a significantly higher amount of WAS (20 % vs 11 %, $p = 0.032$) in the hyperactive group. Comparing the mixed group and the hypoactive group, we found a significantly higher amount of WAS (19 % vs 11 %, $p = 0.049$) in the mixed group.

DISCUSSION

In this cross-sectional study on hospitalized geriatric patients with delirium, we found a low level of upright activity with no significant differences between the hyperactive, hypoactive and mixed groups. However, the no-subtype group had significantly more upright time than the hypoactive group and a significantly higher number of transitions than both the hypoactive and the mixed groups. In addition, we found significant differences in WAS between the hyperactive, hypoactive and the mixed groups, with higher amounts of WAS in the hyperactive and mixed groups than in the hypoactive group.

To our knowledge, this is the first study to simultaneously measure motor activity as both upright activity and wrist activity in geriatric patients with delirium motor subtyped by use of the DMSS, the only validated tool for motor subtyping. Godfrey conducted the only previous study analyzing motor activity across DMSS-defined motor subtypes, but reported only upright activity[14]. Patients included were substantially younger than our sample (mean age 70.7 years vs 86.7 years), and the overall finding was significant differences between the hyperactive and the hypoactive groups with the mixed group between the other groups. We could not reproduce these findings, probably because our patients are frail with heavily impaired gait function illustrated by a mean SPPB score of 2.7, and on a group level are incapable of expressing hyperactivity through increased amounts of upright activity. For total wrist activity, however, our results complies with Godfrey's with a significant difference between the hyperactive and the hypoactive groups and the mixed group between these. In our material, WAS separates the hypoactive group from both the hyperactive and mixed groups, which complies with the DMSS that states that both the hyperactive and the mixed groups have some sort of hyperactivity. In sum, the results from wrist actigraphy illustrates that also geriatric patients with delirium have motor disturbances that applies with the DMSS and can be captured by use of devices measuring aspects of motor activity other than upright time, and

that wrist activity, especially during sedentary behavior, is a promising motor activity measure in frail, geriatric patients since it is independent of the patient's gait function.

Figure 2 illustrates a large variability within all groups for all measures of motor activity. This probably reflects that factors other than motor subtype also influence motor activity in geriatric patients with delirium, such as acute disease, frailty, brain pathology like Parkinson's disease and vascular dementia, lower limb function and sequels after strokes and amputations. We identified discharge diagnoses with the potential of influencing motor activity in a negative way like strokes, fractures and difficulties to walk due to frailty or subcortical brain pathology in 33 out of 60 patients. In our sample, a low level of physical function is illustrated by low SPPB score in all groups, illustrating that geriatric patients with delirium are hardly able to get out of bed and walk. According to SPPB score, the hyperactive and the no-subtype groups seem to have better physical function, but this might reflect the impact of the motor subtype on the SPPB performance rather than patients' physical function at baseline. When it comes to activity monitoring data, the patients with hyperactive delirium had low levels of upright activity, with a mean value of 79 minutes of upright time and 27 transitions per 24 hours. This illustrates that geriatric patients with delirium, and even those with hyperactive delirium, spend a majority of time in a sedentary position. Thus, clinicians cannot rely on wandering and changing of posture when looking for delirium. Our results indicate that patients with both hyperactive and mixed delirium express hyperactivity through wrist activity, and that clinicians should evaluate signs of restlessness in bed or in a chair rather than judging upright activity when looking for delirium.

This is the first study to report results of an accelerometer-based motor activity analysis in the no-subtype group. Some speculate that the no-subtype group represents less serious, questionable or resolving delirium[13, 27]. In our study, the main finding for this group was a higher amount of upright activity than both the hypoactive and mixed groups. The no-subtype

group spent 119.3 minutes out of 24 hours in upright position, which is almost identical to the 117.1 minutes of a general case-mix of hospitalized geriatric patients that we have recently reported from our ward[16]. This might indicate that the three motor subtypes hyperactive, hypoactive and mixed delirium represent fundamental motor disturbances eventually resulting in reduced motor activity, whereas the no-subtype represents a milder delirium not reaching the threshold for developing motor disturbances and that patients with no-subtype delirium thereby have a higher level of motor activity, more similar to patients without delirium. Thus, the important differences in motor activity in patients with delirium may be between the majority with motor symptoms and the minority without motor symptoms. This view is supported by a study finding that 38 patients with un-subtyped delirium had less wrist activity than 32 patients without delirium during the first 24 hours after cardiac surgery[28]. In sum, the results from studies using activity monitoring in patients with delirium indicate that delirium, in general, is associated with less, and not more motor activity, and also raise the question if the term "hyperactive delirium" is misleading.

Strengths and limitations

The major strengths of this study are the simultaneous use of two accelerometer-based devices to measure both upright activity and wrist activity simultaneously, and the use of DMSS for motor subtyping. This is also the first study to include the no-subtype group in analyses of motor activity. Our patients are old and frail. This is a strength since such patients frequently have delirium and were not recruited in previous research on delirium and activity monitoring, but also a limitation since our results are not necessarily applicable to patients with delirium in other settings. The sample of 60 patients is large compared to the only previous study in the field, although the small number of patients in each subgroup is the major limitation, creating a risk of type II error and preventing firm conclusions. There is also a possibility that patients with the most intense delirium were not included or did not

complete activity monitoring, introducing a possible inclusion bias influencing the results. A potential bias is that patients with hyperactive delirium were slightly overrepresented among those who did not complete 24-hour activity monitoring. Another important limitation is the cross-sectional design. A recent publication indicates that a substantial number of patients with delirium fluctuate between subtypes[27], but we believe this has limited impact on our results since the activity monitoring was done in a limited time-frame centered on the time of diagnosing and subtyping.

Conclusions

In this sample of frail, geriatric patients with delirium, we found a low level of upright activity with no differences between the hyperactive, hypoactive and mixed groups for neither upright time nor transitions. However, we found differences across these groups in both total wrist activity and WAS, indicating that there are true differences in motor activity across DMSS-defined motor subtypes also in geriatric patients with delirium. Our results indicate that restlessness while in a sedentary position is a more reliable clinical feature than wandering and changing of posture when looking for delirium in geriatric patients. Further research should address how motor features can improve the diagnostic work-up of delirium in general and explore possible therapeutic consequences for the different delirium motor subtypes.

FIGURE LEGENDS

Figure 1. Flow chart summarizing reasons why patients did not complete 24-hour activity monitoring.

Figure 2. Box-plots with delirium motor subtypes on the x-axes and time in upright position, sit-to-stand transitions, counts and Wrist Activity in Sedentary position (WAS) in percent of total time in sedentary position on the y-axes. The horizontal line in each box is the median, and the bottom and top of the boxes are the quartiles.

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The material presented in this article was presented as an eight-minute lecture at the European Delirium Association yearly meeting in 2017.

STATEMENTS

Author Contributorship

SE did the initial drafting of the article, had the main responsibility for data collection and for diagnosing and subtyping of delirium

AKB processed and analyzed the activity monitoring data

OS is the project manager and designed the study. He also participated in diagnosing and subtyping of delirium.

SL had the main responsibility for the statistical analyses

IS participated in designing and planning the study with particular responsibility in data collection at the geriatric ward.

TBW participated in designing and planning the study with particular responsibility in the diagnostic work-up of delirium and subtyping.

KT participated in designing and planning the study, with a particular responsibility in planning data collection with the accelerometer-based devices.

All authors have critically read and approved the final manuscript.

Competing interests

Alan Kevin Bourke worked at NTNU, Department of Neuromedicine and Movement Sciences, when completing his contribution to this article. After finishing his contribution, but before the article was submitted, he started working at Roche Pharmaceutical Research and Early Development (pRED), Roche Innovation Center Basel, F.Hoffmann-La Roche Ltt, 124 Grenzacherstrasse, Basel, CH 4070, Switzerland.

The other authors have no competing interests to report.

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Other statements

Data Sharing: Datasets from this study are not available since we do not have the consent to share the data neither from The Regional Committee for Medical and Health Research Ethics nor from the patients.

Patient consent: We confirm that all patients or a proxy consented for participation based on the concept of written informed consent.

Ethical approval: The Regional Committee for Medical and Health Research Ethics of Mid-Norway approved the study (REK Central 2015/474).

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Delirium and motor activity

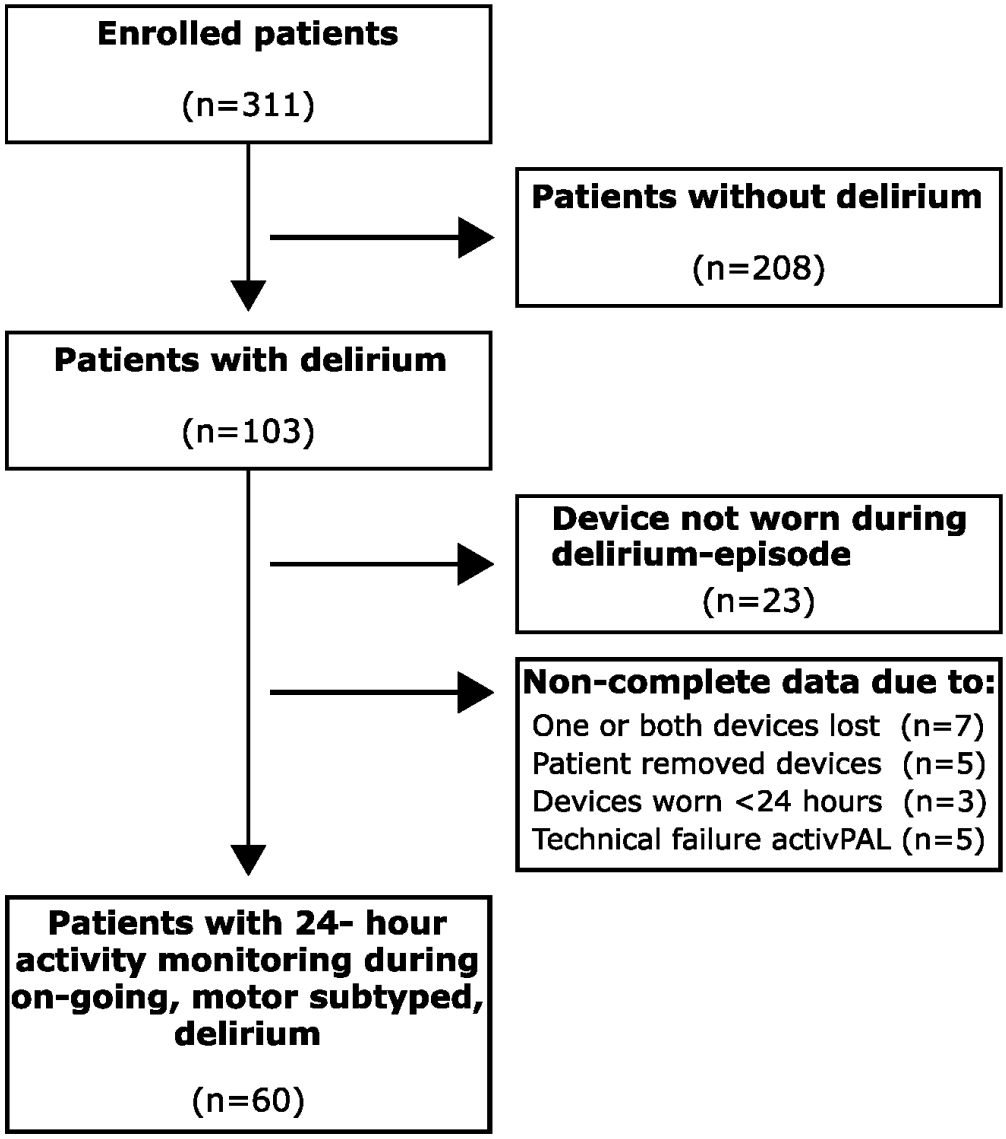

Figure 1. Flow chart summarizing reasons why patients did not complete 24-hour activity monitoring.

111x126mm (300 x 300 DPI)

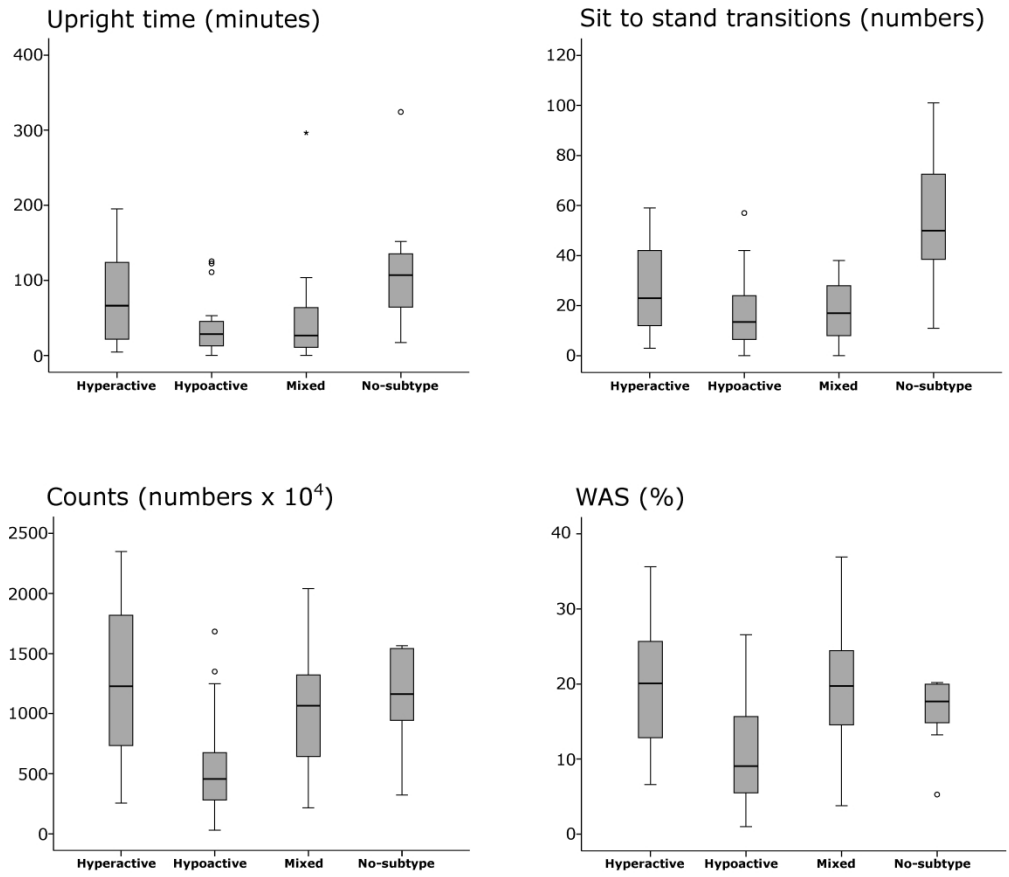

Figure 2. Box-plots with delirium motor subtypes on the x-axes and time in upright position, sit-to-stand transitions, counts and Wrist Activity in Sedentary position (WAS) in percent of total time in sedentary position on the y-axes. The horizontal line in each box is the median, and the bottom and top of the boxes are the quartiles.

356x308mm (300 x 300 DPI)

Reporting checklist for cross sectional study.

Based on the STROBE cross sectional guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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		Reporting Item	Page Number
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	#3	State specific objectives, including any prespecified hypotheses	5
Study design	#4	Present key elements of study design early in the paper	5
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants.	6

	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	6-9
Bias	#9	Describe any efforts to address potential sources of bias	15
Study size	#10	Explain how the study size was arrived at	9
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	9, 45
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	9
	#12b	Describe any methods used to examine subgroups and interactions	9
	#12c	Explain how missing data were addressed	9
	#12d	If applicable, describe analytical methods taking account of sampling strategy	Not relevant
	#12e	Describe any sensitivity analyses	Not relevant
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	9, Fig1
	#13b	Give reasons for non-participation at each stage	9, Fig1
	#13c	Consider use of a flow diagram	Fig 1
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and	Table 1

		unexposed groups if applicable.	
	#14b	Indicate number of participants with missing data for each variable of interest	9, Fig1
Outcome data	#15	Report numbers of outcome events or summary measures. Give information separately for exposed and unexposed groups if applicable.	9, table 2
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12, table 2
	#16b	Report category boundaries when continuous variables were categorized	Not relevant
	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	9, table 2
Key results	#18	Summarise key results with reference to study objectives	13
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	15
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	13-15
Generalisability	#21	Discuss the generalisability (external validity) of the study results	13-16
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19