

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

This paper was submitted to a another journal from BMJ but declined for publication following peer review. The authors addressed the reviewers' comments and submitted the revised paper to BMJ Open. The paper was subsequently accepted for publication at BMJ Open.

(This paper received three reviews from its previous journal but only two reviewers agreed to published their review.)

ARTICLE DETAILS

TITLE (PROVISIONAL)	Motor activity across delirium motor subtypes in geriatric patients assessed using body-worn sensors – a Norwegian cross-sectional study
AUTHORS	Evensen, Sigurd; Bourke, Alan Kevin; Lydersen, Stian; Sletvold, Olav; Saltvedt, Ingild; Wyller, Torgeir Bruun; Taraldsen, Kristin

VERSION 1 – REVIEW

REVIEWER	SANDEEP GROVER Post Graduate Institute of Medical Education and Research
REVIEW RETURNED	14-Oct-2018

GENERAL COMMENTS	From the methodology section, it is not clear at what stage of admission were the patients recruited into the study. Sample size is small to draw any conclusions. Why did the authors limit the recording to 24 hours only requires explanation. The study was limited to frail elderly, which again raises the question about the generalization of the findings. Could the wrist activity be influenced by kind of treatment received during the monitoring, like IV lines and other factors like use of restraint. These facts require clarification. DMSS was used to rate the motor activity, which time frame was taken into account in rating the scale. Were these findings blinded to the findings of the accelerometers ?
-------------------------	-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

REVIEWER	Giuseppe Bellelli Department of Medicine and Surgery, University of Milano-Bicocca, Milan, Italy
REVIEW RETURNED	14-Oct-2018

GENERAL COMMENTS	Delirium is a common and serious condition, yet generally under-researched. Previous studies have shown that the different motor subtypes of delirium carry different prognostic implications for the patients, suggesting that they could represent separate phenotypes and that a lot of research is still required to understand their pathophysiological mechanisms. Therefore the authors are to be congratulated on tackling this difficult area. This is a nice manuscript, clear and logically laid out. I enjoyed reading it. However, I think that there are some flaws which need to be addressed. Here are my comments:
-------------------------	-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

	<p>Introduction section.</p> <p>It is well written and informative.</p> <p>1. 2nd sentence. Please replace “physiological disturbances” with “physiological consequence of an underlying medical condition”</p> <p>Method sections.</p> <p>1. Please report in the method section that you used the STROBE cross sectional reporting guidelines, as required by the journal.</p> <p>2. Selection criteria. It is unclear why living outside the city of Trondheim was an exclusion criterion. Please clarify. It’s also important to know if delirium that was already present on admission to the unit was an exclusion criterion or not. Indeed, without excluding patients with prevalent delirium, it could be hypothesized that patients’ functional performances at baseline may have been affected by an ongoing delirious state, not representing the true patients’ condition at baseline. This would have practical implications not only to the stratification of patients in the 4 subtype groups but also to the characterization of the whole cohort (for example the SPPB score may have been lower in some groups because of delirium). Please clarify this point.</p> <p>3. Diagnosis of delirium. Please specify who did the diagnosis of delirium at the Geriatric Unit and the expertise level in using DSM-5 criteria. As the authors certainly know, this is crucial in order to have an accurate diagnosis. Were the researchers who attached the Actigraph and the ActivPAL blind to the results of the DMSS assessment?</p> <p>4. Forty patients who refused to wear the devices or not completed device’s monitoring over a global cohort of 103 patients with delirium implies an important attrition rate, which may have affected the final results of the study. Page 7. The authors state: “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”. This may represent a potential bias. In fact, it is very likely that many, if not all, of these patients had a severe form of delirium, the most intriguing for such a kind of studies, especially of the hyperactive form. In the strengths and limitations section, the authors acknowledged that patients with the most intense delirium may have not included or did not complete activity monitoring, introducing a possible inclusion bias. However, I think they could be more explicit in saying that the refusal to wear the devices may have masked a severe form of delirium, especially hyperactive.</p> <p>5. Did the authors assess the duration of delirium? This information would also be important to classify in a reliable manner the DMSS group membership, given that increased duration of delirium may be associated with increased likelihood of shifting from one motor subgroup to another (see for example Slor CJ, 2013).</p> <p>6. If I’m not wrong, to assess the DMSS delirium subtypes, it’s required to observe the patient’s activity during the last 24 hours. Can the authors please specify more in detail the timing of assessment of either the DSM-5 defined diagnosis of delirium, the DMSS-defined subtypes and the timing of attaching both devices?</p> <p>Results section.</p> <p>7. The average SPPB score suggests that, on average, patients were severely frail or disabled. This is with no doubt a strength of the study since it reflects a real-world picture of many geriatric units. However, it might also represent a limitation. Why patients</p>
--	--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

	<p>who were so severely impaired in their function would have been motivated (or able) to stand up and move? I mean that performances could be related to the baseline characteristics of the patients rather than to different subgroup's phenotype.</p> <p>8. Table 1. Please explain in a clear manner the meaning of the values in bracket. I suspect that the authors have reported only the SD and not the mean values, with regard to Barthel, GDS, SPPB, etc.</p> <p>Discussion section</p> <p>9. Page 13, penultimate line...there are two "that". Please modify</p> <p>10. As the authors correctly acknowledge in their discussion, poor motor activity may be related to specific medical conditions, such as Parkinson disease, previous stroke and vascular dementia. Please, specify how many of these patients have been enrolled in the research.</p> <p>11. Can the authors try to explain the pathophysiological basis underlying the results of their study?</p> <p>12. The authors assumed that the motor subtype was stable during the 24-hour observation period. They also acknowledged that this may be a potential limitation. I would like to point out that this limitation may be more relevant especially to specific motor subgroups (see for example Scholtens et al 2016), such as no motor subgroup. Can the authors discuss this?</p> <p>References</p> <p>13. The ref no 2 should be corrected.</p> <p>Figure 2. The layout of the figure should be modified.</p>
--	-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

REVIEWER	Neus Gual Tarrada Parc Sanitari Pere Virgili, Barcelona
REVIEW RETURNED	28-Oct-2018

GENERAL COMMENTS	<p>To the authors</p> <p>S. Evensen and colleagues performed a cross-sectional study of delirious patients admitted to a geriatric ward with Medical conditions. The authors used DMSS to identify delirium motor subtypes and data from two accelerometer-based devices to objectively determine the motor activity of those patients. The authors identify no differences in upright activity between hyper, hypo and mixed delirium, but higher significant upright activity in the non-motor delirium subtype. On the other hand, it seems that wrist activity may have a better correlation with the delirium motor subtype in older inpatients. This study targets an under-studied group, with very old and frailty patients with high incidence of delirium, and the interesting results can be useful and applicable to daily routine in geriatric wards.</p> <p>1. P.2, line 33. I would recommend to add some information about the distribution of the delirium motor subtypes in the results section of the abstract because that can help the reader to get a better idea of the study population.</p> <p>2. P.2, line 37. Please add the minutes of the upright time of hypoactive group either. You could do it that way: ...but more upright time for the no-subtype group than the hypoactive group (119.3 vs min.; p=0.042).</p> <p>3. P.6, lines 33-35. In line 12-14, you explain that nurses, physiotherapist and physician were able to include patients. But since using the DSM-5 for diagnosing delirium needs some</p>
-------------------------	---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

	<p>training and can sometimes be difficult, especially in patients with previous dementia. I would recommend to explain better who did the diagnosis of delirium, which training/background/expertise had this person and how have you determined the presence of dementia and that the symptoms were not due to the existing dementia. It is important to perform a detailed assessment of delirium and dementia and to explain it in the manuscript, to assure that you included patients with Delirium superimposed to dementia (DSD) in this study and that all included patients developed delirium.</p> <p>4. In the Activity Monitoring section, it is unclear if patients wear the accelerometer-based devices during all their hospital stay (p.6, line 49-50) or only during 24 hours (p.7, line 14-16). Please clarify.</p>
--	----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1 (Sandeep Grover)

Comment 1: From the methodology section, it is not clear at what stage of admission were the patients recruited into the study.

Answer 1: Thank you for pointing this out. In the second paragraph on page 6, the section “Design, settings and participants”, we have stated that the patients were included within 24 hours after admission. To be quite clear about the time-line we have added “as soon as possible and always...” to this sentence in the second paragraph, page 6.

Comment 2: Sample size is small to draw any conclusions.

Answer 2: We agree that the sample size in this study is small and have already mentioned this as a limitation in the section “strengths and limitations” where we discuss the possibility of type II errors. We have now added “and preventing firm conclusions” to this sentence (page 16, section “Strengths and limitations”).

Comment 3: Why did the authors limit the recording to 24 hours only requires explanation.

Answer 3: We understand the need to clarify this. We have limited the activity monitoring to one midnight to midnight period to be as sure as possible that the patients reported had delirium with a certain motor subtype during the entire period of activity monitoring. We have tried to make this clearer by adding the sentence described at the top of the letter and by Adding the sentence “Only patients with complete 24-hour activity monitoring centered on the time of diagnosis of delirium were included in the final analysis” to the section “Design, settings and participants,” page 6.

Comment 4: The study was limited to frail elderly, which again raises the question about the generalization of the findings.

Answer 4: We agree, and we have already mentioned this in the section “Strengths and limitations.” To clarify, we have rewritten the fourth sentence in this section: “... but also a limitation since our results are not necessarily applicable to patients with delirium in other settings.” (page 16).

Comment 5: Could the wrist activity be influenced by kind of treatment received during the monitoring, like IV lines and other factors like use of restraint. These facts require clarification.

Answer 5: We agree that there is a need to clarify this and have added that the staff attaching the devices made sure they did not interfere with other devices and IV-lines: “, making sure the devices did not interfere with equipment for monitoring and intravenous lines.” (page 7, section “Activity monitoring,”).

There is no use of physical restraints in our ward as we consider restraints counterproductive and harmful. We have added this, and some other information about the ward at the top of page 6, section “Design, settings and participants.” “The ward has only single bed rooms and is built to enhance orientation and physical activity. There is no use of physical restraints.”

Comment 6: DMSS was used to rate the motor activity, which time frame was taken into account in rating the scale. Were these findings blinded to the findings of the accelerometers?

Answer 6: Using the DMSS, we have considered the 24-hour period the activity monitoring took place. We have clarified this in the last sentence in the paragraph “Diagnosis of delirium and motor subtypes,” on the top of page 7, adding “and used all available information from the chosen 24-hour period of activity monitoring when deciding motor subtypes.”

The DMSS assessors were blinded to the findings of the accelerometers as the accelerometers data were analysed after the last patient was discharged. The person (AKB) analysing the activity data was not involved in any other parts of the project. We have specified this by adding “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.” (page 7, “Activity monitoring,”)

Reviewer 2 (Giuseppe Bellelli)

Introduction section.

It is well written and informative.

Comment 1: 2nd sentence. Please replace “physiological disturbances” with “physiological consequence of an underlying medical condition”

Answer 1: We agree and have therefore rewritten the sentence more or less like the reviewer suggests: “...that are physiological consequences of an underlying medical condition (page 4, second sentence of “Introduction”).

Method sections.

Comment 2: Please report in the method section that you used the STROBE cross sectional reporting guidelines, as required by the journal.

Answer 2: We have added this to the last sentence of the section «Statistical analysis» ... “and report the results according to the STROBE cross sectional reporting guidelines,” page 9.

Comment 3: 2. Selection criteria. It is unclear why living outside the city of Trondheim was an exclusion criterion. Please clarify.

Answer 3.1: We understand that this is confusing. This study is part of a larger project that involved four months follow up with cognitive testing of patients with delirium, and therefore living outside Trondheim and the closest municipalities was an exclusion criterion. Since this is not important for the present manuscript, we have removed this information (page 5, second paragraph).

It's also important to know if delirium that was already present on admission to the unit was an exclusion criterion or not. Indeed, without excluding patients with prevalent delirium, it could be hypothesized that patients' functional performances at baseline may have been affected by an ongoing delirious state, not representing the true patients' condition at baseline. This would have practical implications not only to the stratification of patients in the 4 subtype groups but also to the characterization of the whole cohort (for example the SPPB score may have been lower in some groups because of delirium). Please clarify this point

Answer 3.2: We agree – there is a need to specify that also patients with prevalent delirium were included, and we have specified that no patients were excluded due to any diagnoses by adding “We did not exclude any patients due to diagnosis like dementia, prevalent delirium, other neuropsychiatric conditions or sensory deficits” to the second sentence of the second paragraph of the section “Design, settings and participants,” page 6.

We agree that delirium motor subtype probably has influenced each patient's SPPB score, and it is certainly possible that the differences seen in SPPB score across the groups reflect the motor subtype and not the patients' SPPB score when delirium free. We have now mentioned this in the third paragraph of the “Discussion” section page 15, by adding the sentence “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.

However, the inclusion of patients with prevalent delirium does not have implications for other baseline characteristics as none of the other baseline variables are performance based, and we do not think this has implications for motor subtyping since subtyping is based on a combination of interviews and chart reviews.

Comment 4: Diagnosis of delirium. Please specify who did the diagnosis of delirium at the Geriatric Unit and the expertise level in using DSM-5 criteria. As the authors certainly know, this is crucial in order to have an accurate diagnosis. Were the researchers who attached the Actigraph and the ActivPAL blind to the results of the DMSS assessment?

Answer 4: We have specified who did the diagnosis of delirium by rewriting the first sentence in the section «Diagnosis of delirium and motor subtypes” on page 6. “Two experienced 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.”

Furthermore, the devices (Actigraph and ActivPAL) were attached by a nurse or a physiotherapist who did not take part in the DMSS assessment. Therefore, we have rephrased the sentence: “A nurse or a physiotherapist not taking part in diagnosing or subtyping of delirium attached the devices immediately after inclusion” (“Activity monitoring”, page 7).

Comment 5: Forty patients who refused to wear the devices or not completed device's monitoring over a global cohort of 103 patients with delirium implies an important attrition rate, which may have affected the final results of the study. Page 7. The authors state: “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”. This may represent a potential bias. In fact, it is very likely that many, if not all, of these patients had a severe form of delirium, the most intriguing for such a kind of studies, especially of the hyperactive form. In the strengths and limitations section, the authors acknowledged that

patients with the most intense delirium may have not included or did not complete activity monitoring, introducing a possible inclusion bias. However, I think they could be more explicit in saying that the refusal to wear the devices may have masked a severe form of delirium, especially hyperactive.

Answer 5: We agree that this is important. As figure 1 illustrates, only five patients removed the devices: For the rest of the 43 patients we chose to exclude from these analyses there were other reasons for exclusion, usually that the delirium episode was too short and ended before the devices were attached or within the 24-hour period. We agree that these five patients might have had severe hyperactive delirium, but we believe we have already covered these concerns sufficiently with the sentence "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" (section "strengths and limitations," page 16-17). As we have mentioned in the result sections, slightly more patients with hyperactive delirium were excluded from activity monitoring (12 hyper, 10 hypo, 7 mixed, 4 no-subtype), and we have now added this in the section "strengths and limitations," page 17: "A potential bias is that patients with hyperactive delirium were slightly overrepresented among those who did not complete 24-hour activity monitoring."

Comment 6: Did the authors assess the duration of delirium? This information would also be important to classify in a reliable manner the DMSS group membership, given that increased duration of delirium may be associated with increased likelihood of shifting from one motor subgroup to another (see for example Slor CJ, 2013).

Answer 6: This is an important input. We did not assess the duration of delirium beyond the 24 hour period, which certainly is a weakness of the study. Our focus was on the measured activity related to the classification of motor subgroup in a limited time frame. Therefore, we believe that the lack of an estimate for the duration of the delirium episode has limited implications for this manuscript.

Comment 7: If I'm not wrong, to assess the DMSS delirium subtypes, it's required to observe the patient's activity during the last 24 hours. Can the authors please specify more in detail the timing of assessment of either the DSM-5 defined diagnosis of delirium, the DMSS-defined subtypes and the timing of attaching both devices?

Answer 7: These questions were also addressed by reviewer 1 (Comment 4 and 6). We have specified that the assessment of both DSM-5 criteria and the DMSS was based on an interview with the patient supplied with all available information from the 24-hour period the activity monitoring took place, please see page 7, "Diagnosis of delirium and motor subtypes." As mentioned on page 6 ("Design, settings and participants"), all patients were included as soon as possible and always within 24 hours after admittance. As mentioned on page 7 ("Activity Monitoring"), the devices were attached immediately after inclusion.

Then, SE and OS did the diagnostic work-up of delirium and motor subtypes, focusing on the first complete 24-hour period (midnight to midnight) the patients wore the devices. We did it this way to make sure that all patients had motor subtyped delirium diagnosed by visit and chart review in the 24-hour period as reported in this manuscript.

Results section.

Comment 8: The average SPPB score suggests that, on average, patients were severely frail or disabled. This is with no doubt a strength of the study since it reflects a real-world picture of many geriatric units. However, it might also represent a limitation. Why patients who were so severely impaired in their function would have been motivated (or able) to stand up and move? I mean that

performances could be related to the baseline characteristics of the patients rather than to different subgroup's phenotype.

Answer 8: We agree that our patients were severely frail. This is the core of our message – geriatric patients with delirium are frail, and they are not able to show hyperactivity through upright activity, but only through wrist activity. We have discussed that performances could be related to baseline characteristics and not only motor subtype in the “Discussion section” both on page 14 and page 15. On the bottom of page 15 we have also mentioned that this implicates that clinicians should not look for wandering when diagnosing delirium but look for restlessness in bed/chair.

Comment 9: Table 1. Please explain in a clear manner the meaning of the values in bracket. I suspect that the authors have reported only the SD and not the mean values, with regard to Barthel, GDS, SPPB, etc.

Answer 9: We have revised Table 1, trying to make it easier to read (note: we have not tracked the changes, just simply replaced the old table with an updated version). The mean values are the values outside the brackets, the values in the brackets are the SD. This is now specified on the top of the table.

Discussion section

Comment 10: Page 13, penultimate line...there are two “that”. Please modify

Answer 10: Done (page 14)

Comment 11: As the authors correctly acknowledge in their discussion, poor motor activity may be related to specific medical conditions, such as Parkinson disease, previous stroke and vascular dementia. Please, specify how many of these patients have been enrolled in the research.

Answer 11: We agree with the reviewer. Using the discharge diagnoses, we have identified 33 patients in this sample of 60 with ICD 10 diagnoses that probably would influence mobility in a negative way. One had Parkinson's disease, six had acute stroke, eight had a fracture and 18 had the diagnosis R 26.8 which in our ward is used to describe patients with walking disturbances of various reasons, usually frailty or dementia. We have now mentioned this on page 15, the first paragraph, adding “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. Consequently, we have reformulated the next sentence, “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.”

Comment 12: Can the authors try to explain the pathophysiological basis underlying the results of their study?

Answer 12: We agree that the pathophysiology of delirium, and specially delirium motor subtypes, is interesting, but we cannot give an answer to this question since very little is known on this topic. Further, the aim of our project is to study delirium phenomenology, not delirium pathophysiology.

Comment 13: The authors assumed that the motor subtype was stable during the 24-hour observation period. They also acknowledged that this may be a potential limitation. I would like to point out that

this limitation may be more relevant especially to specific motor subgroups (see for example Scholtens et al 2016), such as no motor subgroup. Can the authors discuss this?

Answer 13: Scholtens used DMSS to assess motor subtypes daily and found that 62% of hip fracture patients changed motor subtype during the delirium episode, but the changes usually involved a change to or from no-subtype, and Scholtens argue that this indicates that no-subtype represent resolving delirium. The potential implications of these findings in our study are very wide. An obvious implication is that the patients with no-subtype delirium might have had hyperactive, hypoactive and mixed delirium before entering the study, but this would not interfere with the activity data. Further, there is a theoretical possibility that many patients changed subtype during the 24-hour period, but as far as we know no studies have explored if motor subtypes fluctuate within such short time-frames. There is also a possibility that some patients have improved from their delirium during the 24-hour observation period and drifted into no-subtype delirium for a while. The result could be that the hyperactive, hypoactive and mixed groups have a slightly higher activity level than if there were no subtype fluctuation. Finally, we have to say that this is very uncertain, and therefore we have chosen not to further elaborate on this possibility.

References

Comment 14: The ref no 2 should be corrected.

Answer 14.1: We have checked ref no 2 carefully and have not found anything needing correction.

Figure 2. The layout of the figure should be modified.

Answer 14.2: We have modified the figure according to the requirements from the journal.

Reviewer 3 (Neus Gual Tarrada)

Comment 1: 1.P.2, line 33. I would recommend to add some information about the distribution of the delirium motor subtypes in the results section of the abstract because that can help the reader to get a better idea of the study population.

Answer 1: We agree and have added information about the distribution in the first and second line of the "results" section in the abstract: "...Fifteen had hyperactive, 20 hypoactive, 17 mixed, and eight had no-subtype delirium. (Abstract page 2).

To keep the abstract at 300 words we have done the following changes to the abstract (page 2-3):

- Removed "a sample of" from the last sentence of the section "objectives"
- Rewritten the "result" section "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 (1.238×10^4 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 %, $p=0.049$)." (Abstract, page 2).
- Rewritten the first sentence in the section "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." We have also removed the word "however" from the second sentence in the "Conclusions"

Comment 2: P.2, line 37. Please add the minutes of the upright time of hypoactive group either. You could do it that way: ...but more upright time for the no-subtype group than the hypoactive group (119.3 vs min.; $p=0.042$).

Answer 2: We agree and have rewritten the sentence as the reviewer suggests. "We found more upright time in the no-subgroup than in the hypoactive group (119.3 vs 37.8 minutes, $p=0.042$), but no differences..."

Comment 3: P.6, lines 33-35. In line 12-14, you explain that nurses, physiotherapist and physician were able to include patients. But since using the DSM-5 for diagnosing delirium needs some training and can sometimes be difficult, especially in patients with previous dementia. I would recommend to explain better who did the diagnosis of delirium, which training/background/expertise had this person and how have you determined the presence of dementia and that the symptoms were not due to the existing dementia. It is important to perform a detailed assessment of delirium and dementia and to explain it in the manuscript, to assure that you included patients with Delirium superimposed to dementia (DSD) in this study and that all included patients developed delirium.

Answer 3: We agree and have now specified that the assessors of delirium were two geriatricians who had received supervision by an experienced delirium researcher (TBW), page 6, first sentence in the section "Diagnosis of delirium and motor subtypes." Two geriatricians (SE and OS) who had received supervision by an experienced delirium researcher (TBW)..." In the same section, we have also specified how we diagnosed delirium superimposed on dementia. "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." In the section "Activity monitoring," page 7, we have specified that the nurse/physiotherapist attaching the devices did not take part in diagnosing / subtyping – "A nurse or a physiotherapist not participating in diagnosing and subtyping of delirium attached"... Please also see our answer to reviewer 2, comment 4.

To state clearly early in the manuscript that all 60 patients in this study had delirium, we have now added a sentence about this in the section "Design, settings and participants," page 6. "Only patients with complete 24-hour activity monitoring centered on the time of diagnosis of delirium were included in the analysis.

Comment 4: In the Activity Monitoring section, it is unclear if patients wear the accelerometer-based devices during all their hospital stay (p.6, line 49-50) or only during 24 hours (p.7, line 14-16). Please clarify.

Answer 4: We agree. The patients wore the devices during all their hospital stay, and we have now specified this by adding "Patients wore the devices until discharge." in the section "Activity monitoring," page 7.

As outlined in figure one, many did not complete activity monitoring during their delirium episode for several reasons. In addition, delirium tends to fluctuate and resolve. In this manuscript we therefore report results from the patients who completed activity monitoring during a 24-hour period with a certain delirium subtype, and those 24 hours were the very same day / 24-hour period we did the delirium and motor subtype assessment.

VERSION 2 – REVIEW

REVIEWER	SANDEEP GROVER Post Graduate Institute of Medical Education and Research, Chandigarh, India
REVIEW RETURNED	09-Dec-2018

GENERAL COMMENTS	I have not been able to see my previous comments, hence it is difficult to compare, however, manuscript overall looks fine now.
-------------------------	---------------------------------------------------------------------------------------------------------------------------------

REVIEWER	Giuseppe Bellelli University of Milano-Bicocca, Milan, Italy
REVIEW RETURNED	10-Dec-2018

GENERAL COMMENTS	I think that the authors have done a good job. I've no other comments. The only minor revision should be the correction of reference no 3 (Association AP should be corrected to American Psychiatric Association).
-------------------------	------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

REVIEWER	Neus Gual Parc Sanitari Pere Virgili, Barcelona. Spain.
REVIEW RETURNED	31-Dec-2018

GENERAL COMMENTS	The authors have addressed all of my comments and I recommend to accept the paper.
-------------------------	------------------------------------------------------------------------------------

VERSION 2 – AUTHOR RESPONSE

References. As requested by reviewer number 2 we have changed reference number 3 from “Association AP” to “American Psychiatric Association.”

Other corrections

Page 3. We have removed the dot from the end of the first bullet point to make it in line with the other bullet points.

Page 5. We have changed “sequels of stroke” to “sequels after stroke.”

Page 9. We have changed the heading “Statistical analyses” to “Statistical analysis.”

Page 11, table 1. We have change the font of the words / brackets (years) and (no) from bold to normal.

Page 14. We have added a comma, the fifth line from the bottom.

Page 15. We have changed “diagnosis” to “diagnoses.”

Page 15. “SPPB” was misspelled and this is now corrected from “SBBP” to “SPPB.”

Page 16. We have added the words “that patients with no-subtype delirium...”

Page 19. Author contributionship. We have added “of” and corrected “analysed” to