INTRODUCTION

Patients with a delirium after cardiac surgery frequently show a disturbed 24-hr motor activity pattern, with increased motor activity during the night. At the clinical level, a distinction can be made between hyperactive, hypoactive or mixed subtypes of delirium,\(^1,2\) with presumed differences in underlying pathophysiology and responsivity to therapeutic interventions.\(^2\) The hypoactive subtype of delirium is usually poorly recognized.\(^3,4\) At present, data regarding motor restlessness, disturbed circadian rest-activity patterns, and delirium subtypes are based on assessments by means of validated rating scales such as the Delirium Rating Scale-Revised-98 (DRS-r98),\(^5\) or on medical file reports of clinicians or nurses regarding episodes of extreme restlessness of the patient. However, objective and quantitative data of normalization of circadian rest-activity patterns of patients following elective cardiac surgery is lacking, let alone of patients who develop a delirium after cardiac surgery.

Wrist-actigraphy can be used as an objective method to assess 24-hr patterns of spontaneous motor activity for prolonged periods of time in various environments. The method accurately distinguishes rest from activity periods in a valid and reliable way.\(^6,7\) Considering the clinical importance of disturbed circadian rest-activity patterns in delirium after cardiac surgery, clarification of its role has relevance for diagnostic purposes, for early recognition of subtypes of delirium which may improve prognosis by early treatment, and for the development of effective treatment strategies. Therefore, we performed an observational study to explore the usefulness of wrist-actigraphy to quantify characteristics of 24-hr motor activity patterns during a 5-day post-operative period after elective cardiac surgery in patients who did or did not develop a delirium. As a first approach, we focused on the duration of the delirium in relation to recovery of circadian rest-activity patterns.

METHODS

Subjects: we studied 85 patients of 65 years and older who underwent elective cardiac surgery (coronary artery bypass graft, valve surgery, or both) at the department of Cardiothoracic Surgery of the Erasmus Medical Center in Rotterdam. Patients were excluded from the study when ‘deep cooling’ or ‘circulator arrest’ were applied as surgical techniques, when surgery was on an emergency basis, or when signs of pre-operative dementia or delirium were present. The diagnosis delirium was assessed and evaluated daily by a senior psychiatrist and/or trained researchers based on the criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR)\(^8\) and the four-item diagnostic Confusion
Assessment Method- Intensive Care Unit (CAM-ICU). In case the patient was diagnosed as delirious, severity of the delirium was assessed by means of the Delirium Rating Scale-revised 98 (DRS-r98; Dutch translation: Sno and van der Mast).

Subjects were excluded from the present analyses if they were comatose or developed a delirium unrelated to cardiac surgery. Only a post-operative delirium lasting more than one day was judged to be clinically relevant, because of the frequently occurring protracted effects of anesthetic or sedating drugs in elderly patients. The patients were divided into 3 groups: 1) a group with non-clinically relevant delirium, consisting of patients who did not develop a delirium or were delirious only during the first post-operative day (‘Non-cr-Del’; n=46; 26 males; mean age=72.9 years, SD=4.9), 2) a group with a post-operative delirium of short duration, consisting of patients who were delirious for 2 or 3 days directly following surgery (‘Short-Del’; n=16; 9 males; mean age=75.2 years, SD=4.1), and 3) a group with a sustained post-operative delirium, consisting of patients who were delirious for 4 days or more directly following surgery (‘Sustained-Del’; n=17; 9 males; mean age=75.2 years, SD=4.5).

The study protocol was approved by the Medical Ethical Committee of the Erasmus Medical Center and conducted in accordance with the criteria of Good Clinical Practice (Declaration of Helsinki 1964).

Actigraphic measurement and analyses: as soon as the patients returned from surgery to the ICU (usually in the afternoon), the actigraph was placed on the non-dominant wrist for continuous measurement during a period of maximally 6 days. The Actiwatch(r) actigraph (Cambridge Neurotechnology Ltd, Cambridge, UK) (size 27 x 26 x 9 mm; weight 16 gm) contains a piezo-electric acceleration sensor and counted the number of suprathreshold movements (> 0.05 g acceleration) per 1 minute epochs. For the present analyses, the following non-parametric circadian rhythm parameters were computed, per consecutive 24-hr period, starting at 19.00 hrs on the day of surgery: a) L5: activity during the least active 5 hr period in a 24-hr period (starting at 19 hrs on the day of surgery); b) M10: activity during most active 10 hr period in a 24-hr period; and c) Amplitude: difference between M10 and L5. L5, M10, and the Amplitude were computed for each sequential 24-hr period during the post-operative week. In this paper, only Amplitude data are presented as indicator of recovery of circadian rest-activity pattern.

Statistical analysis: we limited our analyses to the first 5 days after surgery because several of the patients were already moved to another hospital / ward after a post-operative period of 4 or 5 days depending on recovery speed or occurrence of complications. Normality of distribution of our parameters was established by means of Kolmogorov-Smirnov tests. In order to determine whether recovery of 24-hr motor activity amplitude during the post-operative days was different between the patient groups, Huynh-Feldt corrected ANOVA’s for repeated measurements were performed with between-subject factor Group (Non-cr-Del, Short-Del, Sustained-Del), within-subject factor Time (5 sequential days or time points), and the interaction between factors Group and Time. In the case of a significant effect, post-hoc Scheffé tests were used to determine specific differences between groups. All analyses were performed with SPSS for Windows (version 13.0). A p-value of <.05 was used to indicate a significant effect or difference.

RESULTS

Delirium severity: delirium severity (DRS-r98) in the Short-Del group decreased, on average, from 24.8 (10) to 5 (5) after 5 days. In line with our definition of this group, a clear
improvement after day 3 was observed. The Sustained-Del group only showed minor improvement of delirium severity from day 1 to day 5: from 19.1 (9) to 16.3 (10).

**Activity Amplitude:** A significant effect was found for factors Group (F(2,63)=3.3, p=.044), Time (F(2.5,157)=29.5, p<.001), and the interaction effect between factors Group and Time (F(4.9,157)=2.8, p=.019); during the 5 post-operative 24-hr periods, mean Amplitude levels were overall higher for the Non-cr-Del group and the Short-Del group, and increased more in these groups as compared to the Sustained-Del group (table 1).

<table>
<thead>
<tr>
<th>Activity Amplitude Mean (SD)</th>
<th>Non-cr-Del Mean (SD)</th>
<th>Short-Del Mean (SD)</th>
<th>Sustained-Del Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24-hr period</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>1</td>
<td>1842 (1396)</td>
<td>2030 (1660)</td>
<td>1310 (1117)</td>
</tr>
<tr>
<td>2</td>
<td>3037 (2294)</td>
<td>2366 (2101)</td>
<td>1904 (1304)</td>
</tr>
<tr>
<td>3</td>
<td>4249 (2682)</td>
<td>3644 (3647)</td>
<td>2657 (2307)</td>
</tr>
<tr>
<td>4</td>
<td>5197 (2655)</td>
<td>5028 (3856)</td>
<td>2112 (1966)</td>
</tr>
<tr>
<td>5</td>
<td>6288 (4042)</td>
<td>5833 (3688)</td>
<td>2785 (2557)</td>
</tr>
</tbody>
</table>

Table 1. Mean (SD) values of the motor activity amplitude (difference between L5 and M10) of the 5 sequential 24-hr periods in post-operative delirium.

**DISCUSSION AND CONCLUSION**

In order to clarify the importance of disturbed motor activity patterns in delirium after cardiac surgery, we explored the usefulness of wrist-actigraphy to objectively quantify characteristics of 24-hr motor activity patterns during a 5-day post-operative period in patients who did or did not develop a delirium after cardiac surgery. As a first approach, rest-activity amplitude characteristics were studied in relation to the duration of the delirium episode. All patients tolerated the wrist-actigraphy well and showed no signs of discomfort. The activity Amplitude (difference between M10 and L5, i.e., difference between day and night-time activity) was found to be significantly higher for the patients in which delirium was absent or with short delirium episodes (≤3 days), and to increase more during the subsequent days in these groups as compared to patients with sustained delirium episodes (≥4 days). The time-dependent increase in activity Amplitude in the patients with no delirium or a non-clinically relevant post-operative delirium reflected a gradual normalization of circadian rest-activity patterns, associated with physical recovery and increase of daytime mobility (post-hoc analyses revealed a significant time-dependent increase in M10, but not in L5). Sustained delirium episodes were, however, accompanied by a continued disturbance of circadian rest-activity patterns.

Variability of our motor activity parameter was high, in all patient groups. Large inter-individual differences also exist in 24-hr motor activity patterns of healthy subjects, which, among others, may reflect influences of age, gender, job-related activities, and personality. In this study, the measurement environment and daily routines were similar for all subjects, and the subjects were 65 years or older. Still, variability was high. Inter-individual differences in pre-surgery activity level and physical condition, and daily fluctuations in severity of illness, medical complications, and medication use may all have contributed to the high variability, irrespective of the presence of a delirium.
We studied actigraphy in relation to the duration of the delirium. Subjects who did not develop a delirium or showed no clinically relevant delirium were used as control group. A brief delirious episode frequently occurs as a result of the recovery from the anaesthesia; in general, this period is considered to be too short to justify the clinical diagnosis of a post-operative delirium. Yet, in future research, it may be relevant to separate these two groups, in order to discover potential differences in the initial recovery phase directly after surgery. In addition, we made no distinction between subtypes of delirium, but focused on the duration of the delirium instead. It is our impression that DRS-r98 ratings emphasize isolated incidences of restlessness or uncontrollable behavior in subtyping the delirious patients as hyperactive or mixed (because these incidences draw the attention of clinicians and nurses), whereas wrist-actigraphy emphasizes overall patterns of rest and activity. In a larger sample, characteristics of the hyperactive, hypoactive, and mixed subtypes of delirium based on quantification by the DRS-r98 are interesting to analyze in relation to specific actigraphy parameters. Presently, we conclude that, dependent upon the duration of the delirious episode, recovery of circadian rest-activity patterns is severely diminished in delirium after cardiac surgery.

REFERENCES