Rapid eye movement activity before spontaneous awakening in elderly subjects

G. FICCA 1, S. SCAVELLI 2, I. FAGIOLI 2, S. GORI 3, L. MURRI 3 and P. SALZARULO 2

1Department of Psychology, Second University of Naples, Naples, 2Department of Psychology, University of Florence, Florence and 3Department of Neuroscience, Institute of Neurology, University of Pisa, Pisa, Italy

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SUMMARY

Previous research in young subjects found that rapid eye movement (REM) density is higher in those REM phases which are followed by an awakening (REM-W) than in those preceding NREM (REM-N), suggesting a ‘gating role’ of REM sleep toward the awakening. It is not yet known whether this evidence is maintained in elderly subjects, who display, relative to young subjects, more awakenings, different sleep states from which the awakenings come (NREM in a high proportion of cases) and a general impairment of rapid eye movement activity (REMA). To investigate this issue, we have compared in three different age groups (young, old and ‘old old’ subjects) the features of REMA, including REM density and the amount and duration of REM bursts, between REM-W and REM-N. Whereas in the young REM density is higher in REM-W than in REM-N, this difference is already reduced in the old group and fully cancelled in the old old subjects. The evidence that old individuals spontaneously wake up despite the absence of an increase of REMA could imply that in the aged awakening is not preceded by an increase of the arousal level (expressed in REM sleep by the REMA). The similar duration of REM bursts for REM-W and REM-N in both groups of old subjects suggests that with age a marked impairment occurs in the organizational aspects of REMs, independently from the following state.

KEYWORDS awakening, elderly, rapid eye movements, sleep

INTRODUCTION

Elderly individuals display impressive changes in the features of spontaneous awakenings. Not only do they wake up more than subjects at other ages (Bliwise 1993; Webb 1982) but they also show longer durations of the awakenings (Akerstedt et al. 2002; Garma et al. 1981) and different frequencies of awakening from each sleep state. In fact, whereas spontaneous awakenings come mainly from rapid eye movement (REM) sleep in young subjects (Campbell 1975), in the elderly they emerge both from REM sleep and from stage 2 (Dijk et al. 2001; Murphy et al. 2000; Salzarulo et al. 1999).

Correspondence: Piero Salzarulo MD, Department of Psychology, University of Florence, Via San Niccolò 93, 50125 Florence, Italy. Tel.: +39-055-2491604; fax: +39-055-2345326; e-mail: salzarulo@mail.unifi.it

The relationship between awakening and REM activity has been convincingly shown by Barbato et al. (1994), who found that in young subjects REM density is higher when REM phases are followed by an awakening relative to the uninterupted ones, suggesting that this parameter is an expression of a gating role of REM sleep for the awakening.

It is not yet known whether this relationship is maintained in elderly subjects, who display, beyond a different pattern of awakening relative to young individuals, also a number of relevant changes in rapid eye movement activity (REMA). Whereas in some studies the quantitative aspects of REMs in the elderly were found to be quite preserved (Ehlers and Kupfer 1989; Feinberg 1974; Ficca et al. 1999), an investigation carried out in older subjects, aged 77–98 years, described a significant reduction of REM density compared with young subjects (Vegni et al. 2001). In addition, both Ficca et al. (1999) and Vegni et al. (2001) studies showed that meaningful
changes occur, across elderliness, with regard to the organizational aspects of REMA, i.e. the tendency of REMs to cluster into bursts.

The aim of this study is to assess, by comparing REMA (both REM density and REM bursts) in REM phases followed by an awakening (REM-W) with those followed by NREM sleep (REM-N), whether in the elderly REM intensity act with a similar ‘gating role’ toward awakening as in young subjects.

METHOD

Subjects

Three groups of subjects were selected for the study: (a) ‘Young’ (Y), \(n = 16\), age range: 20–25 years, \(M = 11, F = 5\); (b) ‘Old subjects’ (O), \(n = 9\), age range: 62–74 years, \(M = 7, F = 2\); (c) ‘Old old subjects’ (OO), \(n = 10\), age range: 77–98 years, \(M = 2, F = 8\). Inclusion criteria were the absence of any major somatic and psychiatric illness and of any complaint about sleep disorders.

Procedure

Subjects were submitted to a single conventional night polysomnography, including: bipolar electroencephalogram (EEG) (Fp1-C3, C3-O1, Fp2-C4, C4-O2), vertical and horizontal electrooculogram (EOG), chin electromyogram, electrocardiogram and respiratory rhythm (Ficca et al. 1999; Vegni et al. 2001). Coffee, alcohol and drugs were not permitted during the experiment.

All sleep recordings were visually analyzed according to conventional rules (Rechtschaffen and Kales 1968). Spontaneous awakenings were defined as at least two consecutive minutes of Stage Wake: this definition has been used in previous studies (Ficca et al. 1999; Salzarulo et al. 1999).

Analysis of eye movements

Eye movements were detected via EOG techniques. According to the methodology described in Ktonas et al. (1990), the vertical component of an eye movement (vertical EOG channel) was detected via the combination of two electrodes, one located supraorbitally and the other infraorbitally, on a vertical plane in the middle of the left eye. As for the horizontal EOG component, it was detected through the combination of two electrodes located laterally to the outer canthus of each eye.

The analysis of REMA features was performed manually by splitting each EOG recording into 1-s epochs and by identifying those epochs without REMA (‘0’ epochs) and those with the presence of well-defined REM-related EOG activity in either EOG channel exceeding a minimum amplitude threshold of 50 \(\mu\)V (‘1’ epochs). Eye movement detection was visually performed by a single scorer who was blind to subjects’ age group. Afterwards, in order to calculate the second-order parameters of REMA, that is their clustering and the characteristics of the REM bursts, the strings of ‘0’ and ‘1’ epochs were submitted to a further analysis: each ‘1’ epoch was assigned to a ‘B’ (= burst) state if it followed within a given time window (fixed in 2 s) a previous epoch also scored as ‘1’. Otherwise, it was assigned to an ‘NB’ (= non-burst) state. The 2-s time window was chosen in agreement with previous studies (Boukadoum and Ktonas 1988; Ficca et al. 1999; Ktonas et al. 1990; Vegni et al. 2001), where it turned to be appropriate for the analysis of clustering pattern.

Statistical analysis

The following measures of REM activity were submitted to two-way ANOVAs taking 'age' and 'state' (REM-W or REM-N) as factors:

(a) REM sleep period duration (min);
(b) number and percentage of REMs in the burst state;
(c) REM density, defined as the percentage of ‘1’ epochs out of the total number of REM epochs;
(d) duration of the REM burst, defined as the time interval between the first and the last ‘1’ epoch of the burst.

Where significant \(F\)'s were yielded, we applied post-hoc comparisons by means of Student's \(t\)-test for unpaired samples.

RESULTS

Sleep measures

Total sleep time, sleep efficiency, proportion of REM sleep and number of night awakenings for all groups are displayed in Table 1.

Duration of REM phases

The duration of REM phases is neither affected by age (Y: 17.8 ± 12.7 min; O: 15.8 ± 9.1 min; OO: 12.7 ± 7.2 min; \(F_{2,125} = 1.5,\) n.s.), nor by the sequence (REM-W: 14.7 ± 11; REM-N: 16.7 ± 11.4; \(F_{2,125} = 0.8,\) n.s.).

Table 1 Main sleep measures in each age group

<table>
<thead>
<tr>
<th></th>
<th>Young</th>
<th>Old</th>
<th>Old old</th>
<th>(F_{2,32})</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total sleep time (min)</td>
<td>420.6 ± 50.3</td>
<td>319.5 ± 73.9</td>
<td>316.8 ± 76.4</td>
<td>10.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sleep efficiency</td>
<td>93.3 ± 5.7</td>
<td>71.9 ± 14.5</td>
<td>63.1 ± 19.7</td>
<td>17.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>REM (%)</td>
<td>19.5 ± 7.4</td>
<td>14.8 ± 5.4</td>
<td>13.7 ± 3.9</td>
<td>3.4</td>
<td>0.047</td>
</tr>
<tr>
<td>Night awakenings (n)</td>
<td>1.9 ± 2.1</td>
<td>6.9 ± 3.2</td>
<td>4.7 ± 2.1</td>
<td>12.9</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Number and percentage of REM bursts

The number of REM bursts significantly decreases with age (Y: 26 ± 19.5; O: 24.2 ± 20.7; OO: 10.9 ± 8.4; \( F_{2,125} = 7.73, P = 0.0007 \)). According to post-hoc contrasts, there is a significant difference between Y and OO (\( P < 0.001 \)) and between O and OO (\( P = 0.007 \)), whereas the difference between Y and O is not statistically significant.

No difference is found between REM-W and REM-N (respectively, 22.9 ± 20.3 and 21.3 ± 17.9; \( F_{1,125} = 0.18, n.s. \)).

In addition, the percentage of REMs in burst (see Fig. 1) is significantly affected by age (Y: 62 ± 13%; O: 59.6 ± 12.2%; OO: 35.3 ± 15%; \( F_{1,125} = 42.81, P < 0.0001 \)). Post-hoc comparisons show a significant difference between Y and OO (\( P < 0.001 \)) and between O and OO (\( P < 0.001 \)); instead, no difference exists between Y and O.

The percentage of REM burst is not significantly different between REM-W and REM-N (respectively, 57.2 ± 18.3 and 53.6 ± 17.4; \( F_{1,125} = 1.48, n.s. \)).

REM density

The REM density globally decreases with age (Y: 13.6 ± 6.8; O: 12.1 ± 6.1; OO: 7.2 ± 4.7; \( F_{2,125} = 19.6, P < 0.0001 \)). According to post-hoc contrasts, there is a significant difference between Y and OO (\( P < 0.001 \)) and between O and OO (\( P = 0.002 \)), whereas the difference between Y and O is not statistically significant. REM density in REM-W sequence is higher than in REM-N (respectively, 13.8 ± 7.8 and 10.8 ± 6.1; \( F_{1,125} = 5.6, P = 0.02 \)).

The decrease with age of REM density has a larger amplitude for REM-W than for REM-N (interaction between the two main factors: \( F_{2,125} = 4.9, P = 0.01 \)). According to post-hoc contrasts, a significant difference between REM-W and REM-N is found only in Y (\( P = 0.001 \)), whereas a difference just failing statistical significance is observed in O (\( P = 0.06 \)) (see Fig. 2).

Duration of REM bursts

The duration of REM bursts remarkably reduces across age (Y: 4.7 ± 2.2; O: 4.1 ± 1.4; OO: 2.0 ± 1.0; \( F_{2,125} = 30.5, P < 0.0001 \)), with post-hoc contrasts indicating that the value in old old subjects is significantly lower than in old and young subjects.

The gradual decrease with age of REM bursts duration similarly concerns REM-W (Y: 6.3 ± 2.6; O 4.2 ± 1.2; OO: 1.7 ± 0.4; \( F_{2,91} = 17.9, P < 0.0001 \)) and REM-N (4.4 ± 1.9; O: 3.9 ± 1.8; OO: 2.1 ± 1.2, \( F_{2,34} = 14.3, P < 0.0001 \)).

As a matter of fact, from Fig. 3, showing the average duration of REM bursts in REM-W and REM-N for each age group, the interaction observed between the two main factors comes clear (\( P = 0.003 \)), as only in Y the duration of bursts is higher in REM-W than in REM-N (\( P = 0.003 \)), whereas there is no significant difference between REM-W and REM-N in O and OO.
DISCUSSION

In agreement with previous investigations (Ficca et al. 1999; Vegni et al. 2001) our data show that age exerts an effect on REM density, but that this effect is still slight in the elderly subjects before 74 years and becomes much more pronounced only in the old old subjects. Interestingly, the decrease is mainly accounted for by a clear diminution of REM density only for those phases followed by an awakening, whereas the decrease with age found in REM phases introducing a shift to NREM sleep has a much smaller amplitude. As a consequence, whereas in the young REM density is higher in REM-W than in REM-N, this difference is already reduced in the old group and fully cancelled in the old old subjects.

In other terms, the loss of the ability to increase REMA in our elderly subjects (both the old and the old old groups), would be especially associated to a particular frame, i.e. the REM phases in proximity of an awakening. It looks as if the propensity to wake up becomes with aging not only irrespective of the sleep state (REM or NREM) in which the subject is (Dijk et al. 2001; Salzarulo et al. 1999) but also of the phasic activity within the REM sleep state.

Aserinsky (1967) showed that the increase of REM intensity was associated to EEG and autonomic system activation. The notion that REM phasic activity changes parallel those of the central nervous system (CNS) arousal level was further supported by Feinberg et al. (1987). According to Barbato et al. (1994), the increase of REMA before awakening reflects the activation of a brain arousing system, ultimately leading to awakening.

Thus, the fact that old individuals spontaneously wake up despite the absence of an increase of REMs could imply that no such arousing process has preceded the awakening.

This is consistent with the possibility, already evoked in some of our past contributions (Akerstedt et al. 2002; Salzarulo et al. 1999), that elderly subjects’ awakening often intervene not as the termination of a natural process, involving the dissipation of the sleep drive and indexed by the rise in REMs, but as an interruption due to the inability of CNS to maintain coordinated and stable activities, the so-called ‘functional uncertainty’ (Salzarulo et al. 1997).

The increased level of sympathetic tone found in elderly subjects sleep (Vitiello et al. 1983) could be an additional factor which enhances the probability of awakening, even after REM periods with low eye movement activity.

In addition, the organizational aspects of REMA are impaired by aging, as shown by the significant age effect detected for all the organizational parameters. Once again, this effect is entangled with the one given by the sequence (REM–awakening versus REM–NREM), because the changes have globally a greater amplitude for REM-W relative to REM-N.

Differently from REM density, however, the impairment in the generation of sufficiently long bursts is selective for REM-W only in ‘young old’ subjects. As aging continues, the physiological frame becomes less relevant and disorganization will remarkably affect also the REMA in REM-N. This indicates that the observed shortening of REM bursts, consistent with Vegni et al. (2001) results can be attributed also to a global impairment in the ability to organize REMs per se, rather than only to a change in the REMA–awakening relationship, with a different proportion between the two factors as a function of age.

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REFERENCES


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