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Title: Impact of alfa delta sleep, but not obstructive sleep apneas on potential cardiotoxic CD4 lymphocytes

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Body: Introduction: Obstructive sleep apneas (OSA) are known to affect immune functions, but the role of sleep patterns like the alpha delta sleep (AD-sleep) have not been addressed. Perforin (P) and/or granzyme-B (GrB) positive CD4 lymphocytes (CD4+) have been linked to the instability of atherosclerotic plaques. Here we report preliminary results suggesting that alpha-delta sleep and not OSA affect cytotoxic CD4+ T cells. Methods: 80 participants were included. According to the apnea/hypopnea index (AHI) groups were classified as controls (C=AHI<15) and OSA (O=AHI =/> 15/h). AD-sleep was defined as > 40% of slow wave sleep with superimposed alpha-rhythm. Intracellular P and GrB in CD3+CD4+ lymphocytes were investigated by standard flow cytometry analysis. Results are shown as means +/- SEM. A p< 0.05 was considered statistically significant. Results: Age and BMI were similar between the 4 groups. Table 1 shows the main results.

| AHI | AHI < 15/h (n=44) | | AHI => 15/h (n=36) | |
|---------------|-------------------|------------|--------------------|------------|
| AD sleep | No AD (n=29) | AD+ (n=15) | No AD (n=30) | AD + (n=6) |
| % of P+ cells | 5.39+/-1.16 | 3.0+/-1.36 | 4,48+/-1,1 | 2,22+/-1,1 |

Mean percentage of P+ or GrB+ cells within the CD3CD4 subset. * = p<0.05

Discussion: To our knowledge this is the first study to report an influence of AD sleep on cytotoxic lymphocytes. While CD4+ cells have limited cytotoxic potential, they might be important in coronary heart disease and viral defense. AD sleep is common in patients with non-restoring sleep like fibromyalgia or chronic fatigue (CF). Our results might help understanding why patients with a CF show a reduced cytotoxic response. An impact of OSA on these cells was not confirmed. This work was supported by Fundação e a

