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EUROPEAN DELIRIUM ASSOCIATION

Evaluation of circulating miRNA in serum samples of delirium patients in acute geriatric medical setting: insights on the inflammatory hypothesis of delirium

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INTRODUCTION

MicroRNA (miRNA) are short non-coding RNA molecules usually composed of 18–25 nucleotides that play a role in the regulation of the neuroinflammation, however its association with delirium is not yet established. Acute medically-ill older patients are at high risk to develop delirium, which is frequently related with adverse outcomes. In this ongoing study we are testing the hypothesis of acute neuroinflammatory response as a disease marker of delirium, measured by serum biomarkers such as miRNA.

Aim: To determine whether elderly patients who develop delirium have a different pattern of inflammatory response than patients without delirium.

METHODS

A case-control prospective study was developed on subjects aged 65 or over, unplanned admitted to Internal Medicine wards, with acute systemic infection. Patients are classified in four groups, according to their cognitive status: no delirium and no dementia (controls), delirium only, dementia only and delirium superimposed on dementia. We also collect blood samples to measure inflammatory mediators, namely levels of miRNAs in circulating monocytes and in exosomes. Serum levels of miRNA were determined by quantitative real-time PCR (qRT-PCR).

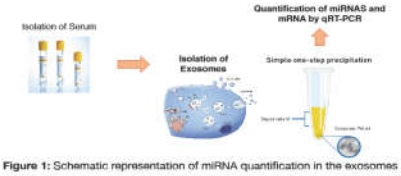

Figure 1: Schematic representation of miRNA quantification in the exosomes

RESULTS

A total of 23 patients (61% female, mean age 85.3±6.1 years - min. 72 years, max. 96 years) (fig.1) were enrolled in this study: 10 controls, 2 delirium only, 5 dementia only and 6 delirium superimposed on dementia.

Cognitive impairment was present in 59% of the sample. Only controls differed significantly from the remaining groups in MoCA test (Mann-Whitney U = 0.0, Z = -2.167; -2.847; -3.277, p <. 05).

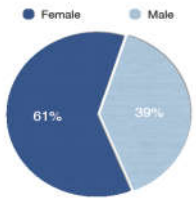

Figure 2: Gender distribution

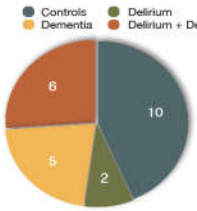

Figure 3: Sample description

Group	Mean	SD	Median
Control	18.3	3.2	18.0
Delirium	5.5	0.7	5,.5
Dementia	7.8	3.2	7.5
Delirium+Dementia	6.1	2.6	5.0
Total	11.9	6.6	10.5

Table 1: Data regarding MoCA test scores placed by sample groups.

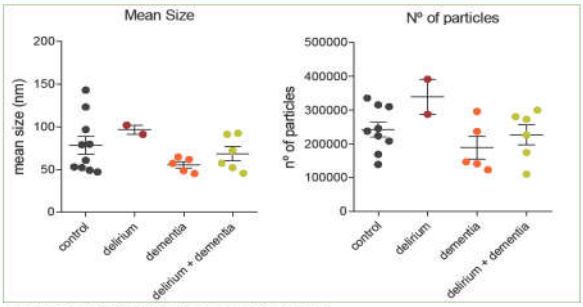

Figure 4: Exosome characterization - dynamic light scattering

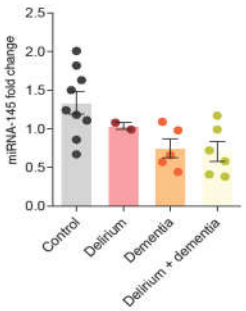

Figure 5: miRNA-145 quantification in the serum exosomes.

Regarding the percentage of exosomes in serum, miRNA-145 is diminished in delirium+dementia group compared to controls (delirium+dementia miRNA-145 fold change=1.18±0.3; controls=2.1±0.56) (fig.5) and the mean size of exosomes in delirium alone is superior than the remaining groups (delirium 95.5±7.6, controls 71.5±10.6, dementia 55.4±5.6; dementia+delirium 68.5±10.8) (fig.4).

CONCLUSION

These preliminary data suggest a down-regulation of miRNA-145 (an anti-inflammatory marker) in serum exosomes of patients diagnosed with delirium+dementia or dementia only. Delirium patients seem to have an increased size of extracellular vesicles when comparing with the other groups.

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