INCREASED SERUM BDNF AND COGNITIVE IMPROVEMENT IN AD PATIENTS TREATED WITH CEREBROLYSIN ALONE OR PLUS DONEPEZIL

A. Alvarez1,2, I. Alvarez1, O. Iglesias2, M. Aleixandre3, C. Linares4, J. Figueroa2,5
1Medinova Institute of Neurosciences, Clinica RehaSalud, A Coruña, Spain. 2Clinical Research Dept., QPS Holdings, A Coruña, Spain. 3Faculty of Psychology, University of Granada, Granada, Spain. 4Faculty of Medicine, University of Malaga, Malaga, Spain. 5Santiago de Compostela University Hospital, Santiago de Compostela, Spain

OBJECTIVES
To investigate the influence of neurotrophic and combination drug therapies on serum Brain-Derived Neurotrophic Factor (BDNF) levels and its cognitive correlates in AD patients.

MATERIALS AND METHODS
The effects of Cerebrolysin (n=52), donepezil (n=52) and a combination of both (n=54) on serum BDNF levels and cognitive performance were investigated in AD patients enrolled in a randomized, double-blind trial.

BDNF levels were measured in serum samples obtained at baseline, at week-16 (end of active Cerebrolysin treatment) and at week-28 (endpoint) by using specific ELISA kits as in previous studies (Alvarez et al., JAD 2014).

CONCLUSION
• Our results suggest the influence of apathy-depression and APOE4 on BDNF metabolism,
• Are in support of a preventive role for BDNF in delaying cognitive decline, and
• Point to the involvement of BDNF in the cognitive effects of Cerebrolysin, at least in AD cases with APOE4.

RESULTS
Baseline BDNF serum levels were significantly lower in APOE4 patients with apathy-depression symptoms than in cases without such symptoms (figure 1).

Cerebrolysin, but not donepezil, increased serum BDNF at week 16, while the combination therapy enhanced it at both week 16 and study endpoint (Table1).

BDNF responses were significantly higher in the combination therapy group than in donepezil and Cerebrolysin groups at week 16 and week 28, respectively (Figure 2).

BDNF increases were greater in patients with apathy-depression and in APOE4 carriers (Table 1).

In APOE4 patients treated with Cerebrolysin, baseline BDNF levels correlated with changes in cognition from baseline to week-16 and to week-28 as evaluated with the ADAScog; and higher BDNF levels at week-16 were associated to greater cognitive improvements at the same time point and predicted a better cognitive performance at endpoint (Figure 3a,b).

Table 1

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Baseline BDNF (ng/ml)</th>
<th>Week-16 BDNF (ng/ml)</th>
<th>Week-28 BDNF (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebrolysin</td>
<td>14.76±1.56</td>
<td>16.61±1.25</td>
<td>19.50±1.25</td>
</tr>
<tr>
<td>Donepezil</td>
<td>14.67±1.96</td>
<td>17.11±1.89</td>
<td>19.26±1.55</td>
</tr>
<tr>
<td>Combination</td>
<td>16.04±1.25</td>
<td>18.88±1.56</td>
<td>19.61±1.12</td>
</tr>
</tbody>
</table>

*p<0.05 vs Baseline; #p<0.05 vs Donepezil

Figure 1

Figure 2

Figure 3

CONCLUSION
• Our results suggest the influence of apathy-depression and APOE4 on BDNF metabolism,
• Are in support of a preventive role for BDNF in delaying cognitive decline, and
• Point to the involvement of BDNF in the cognitive effects of Cerebrolysin, at least in AD cases with APOE4.