Legends supplementary Figures.

Supplementary Fig. 1. Levels of neurodegenerative factors in pEVs from CIND subjects. (A) Levels of $A\beta_{1\text{-}42}$, (B) p-Tau_{181}, (C) t-Tau (D) Ratio of $A\beta_{1\text{-}42}$/p-Tau_{181}. Graph points indicate individual values for each participant. Abbreviations: $A\beta_{1\text{-}42}$, 42-amino acid-long amyloid β peptide; t-Tau, total tau; p-Tau_{181}, hyperphosphorylated tau at Threonine site 181; ApoE, apolipoprotein E; (+), ε4 carriers; (-), ε4 non-carriers; pEVs, plasma extracellular vesicles; CIND, cognitively impaired not demented. Statistical analysis was performed using the student-t test for pEVs t-Tau and the Mann-Whitney test for $A\beta_{1\text{-}42}$, p-Tau_{181} and $A\beta_{1\text{-}42}$/p-Tau_{181} in pEVs. Values are mean ± SEM with $*p < 0.05$ versus CIND-ApoE4(-).

Supplementary Fig. 2. Levels of neurotrophic factors in pEVs and in plasma. Levels of NSE, APP, MMP9 and BDNF measured in pEVs (A, C, E, G) and in plasma (B, D, F, H).
Graph points indicate individual values for every participant. Abbreviations: CIND, cognitively impaired not demented; ApoE, apolipoprotein E; (+), ε4 carriers; (-), ε4 non-carriers; EVs, extracellular vesicles. Statistical analysis was performed using the student-t test for NSE and APP in EVs and the Mann-Whitney test for NSE and APP in plasma as well as MMP9 and BDNF in both EVs and plasma. Values are mean ± SEM with $*p < 0.05$ versus CIND-ApoE4(-).

Supplementary Fig. 3. Levels of neurotrophic and inflammatory factors in pEVs from healthy and CIND-AD subjects. (A) Levels of DJ-1, (B) progranulin, (C) lipocalin, (D) S100B, (E) pentraxin-2, (F) ANGPTL-4. Graph points indicate individual values for every participant. Abbreviations: CTR, controls, CIND-AD, cognitively impaired not demented-Alzheimer's disease; EVs, extracellular vesicles. Statistical analysis was performed using the student-t **test** for DJ-1, progranulin, lipocalin, NPTX-2 and ANGPTL-4 and the Mann-Whitney test for S100B. Values are mean ± SEM.

Supplementary Fig. 4. Statistical correlation between (A) pentraxin-2, (B) α-synuclein levels in pEVs and MMSE scores. Abbreviations: MMSE, Mini-Mental State Examination; r, pearson correlation coefficient; *p*, significance (Student-t test); EVs, extracellular vesicles.