Primary Progressive Aphasia: are measures of amyloid based on cerebrospinal fluid analysis and positron emission tomography interchangeable?

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Background and aim

The use of biomarkers has recently supported the association between Alzheimer's disease (AD) pathology and the logopenic variant of primary progressive aphasia (PPA) (1,2).

We aim to investigate differences in cerebrospinal fluid (CSF) biomarker concentrations in the three PPA variants (i), and to assess the agreement between CSF Aβ42 and amyloid positron emission tomography (PET) (ii).

Methods

A group of 15 PPA patients were retrospectively enrolled between 2016 and 2019. Eight patients were classified as logopenic variant PPA (lvPPA), four as nonfluent/agrammatic variant PPA (nfvPPA) and three as semantic variant PPA (svPPA) (3) (Tab 1).

CSF biomarkers were considered suggestive of AD pathology if Aβ42<550 pg/mL, tau >375 pg/mL, and p-tau >52 pg/mL, according to internal cut-off values. 18(F)-florbetapir or 18(F)-florbetaben images were visually assessed as positive for AD pathology or negative (normal).

Results

Patients with lvPPA showed different mean levels of Aβ42 and p-tau compared to nfv/svPPA (p=0.0001 and 0.01, respectively): Aβ42 206.7 versus 1163.6 pg/ml; p-tau 102.5 versus 50.6 pg/ml. No significant difference was observed for tau concentration between lvPPA and nfv/svPPA patients (i) (Tab 2).

All nfv/svPPA patients had negative Aβ42 and negative amyloid PET. Among the lvPPA group, three of eight patients showed negative Aβ42; notwithstanding two of these three subjects, displaying an incomplete AD profile (high levels of tau and p-tau and borderline level of Aβ42), showed altered Aβ42/p-tau and Aβ42/tau ratios. All lvPPA patients had positive amyloid PET, except the one with a completely normal CSF profile (Aβ42/p-tau and Aβ42/tau ratios also in normal range) (ii) (Tab 3).

Discussion

Our results show that lvPPA patients have a different pattern of CSF Aβ42 and p-tau concentrations compared with the nfv/svPPA group. Interestingly, despite some discordant cases with normal CSF Aβ42 and a positive amyloid PET, an optimal agreement is present when Aβ42/p-tau and Aβ42/tau ratios are considered.

Conclusion

There is a high prevalence of AD pathology in lvPPA cases. Aβ42/p-tau and Aβ42/tau ratios show higher agreement with amyloid PET than Aβ42 alone as markers of AD pathology.

Table 1. Demographic data for all patients and nfv/svPPA and lvPPA patients

	All (N=15)	nfvPPA/svPPA (n=7)	lvPPA (n=8)	p
Age at onset, mean (SD) (ys)	67.0 (10.8)	65.3 (11.9)	68.5 (10.3)	0.58
Disease duration, mean (SD) (mo)	45.4 (31.9)	52.3 (25.1)	39.4 (37.6)	0.20
Gender, n (%) M	9 (60)	5 (71.4)	4 (50)	0.75
F	6 (40)	2 (25.6)	4 (50)	

Table 2. CSF biomarker concentrations in all patients and in nfv/svPPA and lvPPA groups

	All (N=15)	nfvPPA/svPPA (n=7)	lvPPA (n=8)	p
Aβ1-42, mean (SD) (pg/ml)	820.6 (377.1)	1163.6 (204.5)	206.7 (167.2)	0.0001
p-tau, mean (SD) (pg/ml)	78.3 (63.3)	50.6 (10.1)	102.5 (80.5)	0.01
t-tau, mean (SD) (pg/ml)	571.7 (487.1)	353.4 (206.7)	762.7 (590.4)	0.05

Table 3. CSF biomarker concentrations and (18)F-florbetapir PET results in PPA patients

	Aβ42 (pg/ml) (v.n. > 550)	p-tau (pg/ml) (v.n. < 52)	t-tau (pg/ml) (v.n. < 375)	(18)F-florbetapir PET (positive/ negative)
nfvPPA 1	1312	42	164	N/A
nfvPPA 2	1112	42	288	negative
nfvPPA 3	1268	45	356	negative
nfvPPA 4	995	61*	723*	negative
svPPA 5	1275	57*	210	N/A
svPPA 6	1378	42	195	negative
svPPA 7	805	65*	538*	negative
lvPPA 8	375*	90*	1102*	positive
lvPPA 9	583	78*	554*	positive
lvPPA 10	783	48	243	negative
lvPPA 11	404*	81*	613*	positive
lvPPA 12	334*	57*	351	N/A
lvPPA 13	477*	94*	544*	N/A
lvPPA 14	741	74*	610*	positive
lvPPA 15	467*	298*	2085*	N/A

References

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