SALIVARY PROTEIN PROFILE IN DEMENTIA WITH LEWY BODIES

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Introduction

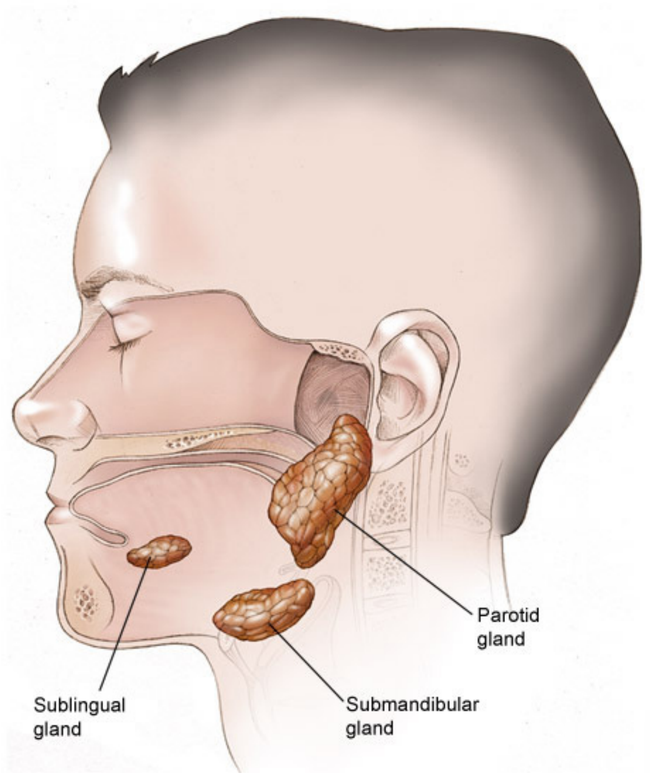
Lewy body diseases (LBDs) such as Dementia with Lewy bodies (DLB) and Parkinson's disease (PD) are neurodegenerative disorders characterized by the deposition of aggregates of misfolded α-synuclein in specific brain structures as well as in peripheral nervous system including paraspinal sympathetic ganglia, the vagus nerve, the gastrointestinal tract.[1] In patients with LBDs, α-synuclein pathological deposits have been found within the nerve fibers of the salivary glands, particularly the submandibular one [2,3].

Objective

In the present study, we aimed to characterize the salivary protein profile of a group of DLB patients in comparison with healthy controls (HC) by a top-down proteomic approach in order to evidence possible quali-/quantitative variations.

Method

Salivary samples were collected from 11 DLB patients and 11 sex and age-matched HC, the protein fractions soluble in acidic solution were analyzed by HPLC-ESI-MS, and peptides/proteins were searched and quantified with a XIC procedure. We analyzed 80 components including proteins/peptides with non-glandular origin (antileukoproteinase, S100 proteins, thymosin b4 and b10, a-defensins, cystatin A and B) and proteins/peptides with glandular origin (acidic proline rich proteins or aPRP, cystatin C, D, S, SN and SA, hystatins, statherin, PB peptide) with all their isoforms and proteoforms originated by phosphorylation, proteolysis, Met and Trp oxidation, Cys glutathionylation, cysteinylation, sulfonylation, nitrosylation, and disulfide dimerization.



Results

DLB patients showed significant higher levels than HC of a truncated proteoform of statherin named SV1, PRP1, and PRP3, PB peptide and its 3 truncated proteoforms, Cystatin S1, S2 , SA and SN, Cystatin D des 1-5, Cystatin B with Cys glutathionylation and cysteinylation and Thymosin b4.

The analysis of salivary protein profile shows that DLB patients, compared to HC, disclose higher concentrations of salivary peptides and proteins that are considered of glandular origin. In particular we observed higher levels of peptides which are mostly or exclusively related to the submandibular gland. The role of submandibular gland in LBDs has not been clearly provided but previous studies have shown a prevalent involvement of this gland, compared to minor salivary glands, in α-synuclein pathology. (2). The higher concentration of peptides observed in DLB patients could be considered a marker of salivary gland dysfunction, which involves, in the case of DLB, mostly the submandibular gland.

Peptide/protein	Glandular Origin	DLB XIC peak area x10^9 mean ± SD (Frequency)	HC XIC peak area x10^9 mean ± SD (Frequency)	DLB VS HC *p* value	
SV1	Submandibular and Parotid	$0.83*10^9 \pm 0.53*10^9$ (11/11)	$0.13*10^9 \pm 0.18*10^9$ (11/11)	< 0.001	DLB ↑
PRP1	Submandibular and Parotid	$6.36*10^9 \pm 3.41*10^9$ (11/11)	$2.81*10^9 \pm 1.54*10^9$ (11/11)	0.03	DLB ↑
PRP3	Submandibular and Parotid	$2.37*10^9 \pm 1.34*10^9$ (11/11)	$1.15*10^9 \pm 0.58*10^9$ (11/11)	0.03	DLB ↑
PB peptide	Submandibular	$1.71*10^9 \pm 0.95*10^9$ (11/11)	$0.61*10^9 \pm 0.52*10^9$ (11/11)	0.002	DLB ↑
Cystatin D (des 1-5)	Submandibular and Parotid	$0.26*10^9 \pm 0.31*10^9$ (9/11)	$0.03*10^9 \pm 0.05*10^9$ (4/11)	0.01	DLB ↑
Cystatin S1	Submandibular	$1.63*10^9 \pm 1.16*10^9$ (11/11)	$0.37*10^9 \pm 0.38*10^9$ (9/11)	< 0.001	DLB ↑
Cystatin S2	Submandibular	$0.48*10^9 \pm 0.33*10^9$ (11/11)	$0.10*10^9 \pm 0.10*10^9$ (9/11)	< 0.001	DLB ↑
Cystatin SN	Submandibular	$3.36*10^9 \pm 1.75*10^9$ (11/11)	$0.57*10^9 \pm 0.57*10^9$ (8/11)	< 0.001	DLB ↑
Cystatin SA	Submandibular	$0.50*10^9 \pm 0.51*10^9$ (8/11)	$0.06*10^9 \pm 0.14*10^9$ (3/11)	0.01	DLB ↑
Cystatin B SSG	Non-glandular origin	$0.10*10^9 \pm 0.06*10^9$ (11/11)	$0.04*10^9 \pm 0.02*10^9$ (11/11)	0.01	DLB ↑
Cystatin B SSC	Non-glandular origin	$0.04*10^9 \pm 0.02*10^9$ (10/11)	$0.01*10^9 \pm 0.009*10^9$ (9/11)	0.008	DLB ↑
Thymosin β4	Non-glandular origin	$0.12*10^9 \pm 0.03*10^9$ (10/11)	$0.03*10^9 \pm 0.05*10^9$ (5/11)	0.009	DLB ↑

Conclusion

Protein profile analysis of the saliva could be used to assess and characterize salivary gland dysfunction in DLB giving new insight on the pathophysiology of the disease.

Refereces

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