BIOLOGICAL VARIATION OF PLASMA SNAP-25 LEVELS IN 23 HEALTHY VOLUNTEERS

Shreyasee Das[1],Julie Goossens[1],Jeroen Vanbrabant[1], Elizabeth Herries[2], Jack Ladenson[2], Eugeen Vanmechelen[1]
[1]ADx NeuroSciences. Gent. Belgium
[3]Departments of Pathology and Immunology and Neurology, Washington University School of Medicine, St. Louis

P0071

INTRODUCTION

Synaptosomal associated protein 25 (SNAP-25) is an emerging Alzheimer's disease (AD) specific synaptic biomarker, although its applications in plasma are in the discovery stage. The brain-specific expression pattern of SNAP25 makes it relevant for consideration as a target-engagement biomarker in AD. In this study, we explored the stability of plasma SNAP-25 over seven months of follow-up, as well as its correlation to other plasma biomarkers NfL, Ptau181, and Aβ42/40 that have recently been recommended for clinical use.

METHODS

Plasma samples at baseline and seven months follow-up were obtained from 23 healthy volunteers (45.7 ± 15.3, 56.5% female) from Anacura (Evergem, Belgium). The plasma biomarkers were quantified with homebrew immunoassays on the Quanterix Simoa™ platform. Immunoassays for Aβ42/40 ratio and PTau181 have been previously described (1,2). while NfL and SNAP-25 were recently developed in-house at ADx NeuroSciences (Gent, Belgium).

RESULTS

Plasma SNAP-25 levels ranged from 0.249 pg/mL to 1.117 pg/mL. In healthy individuals, plasma SNAP-25 levels were stable over 7 months, while NfL increased from baseline to follow-up. The age-dependent increase of NfL was reflected in the follow-up samples which demonstrates a significant (P=0.017) increase in these 23 individuals on the group level. While the SNAP25 levels were stable over time 4 of the 5 individuals demonstrate an increase in SNAP25 levels (Table 1), while Ptau181 or Aβ42/40 were not changed. In the overall cohort, SNAP-25 correlated weakly to plasma Ptau181 (Spearman, rho=0.30, P=0.05), although upon stratification for baseline (Spearman, rho=0.29, P=0.20) and follow-up (Spearman, rho=0.26, P=0.26) sampling phase, this correlation was lost. In contrast to NfL (Spearman, rho=0.45. P=0.001), SNAP-25 levels in plasma were not associated with age.

Table 1: Demographic Characteristics of the 23 healthy volunteers

Volunteer	Age	Follow- up (weeks)	Sex	Sample	SNAP25	$Aβ_{42/40}$	Ptau181	NfL
1	22.0		F	Baseline	0.481	0.183	17.7	11.6
1	22.6	32.7	F	Follow- up	0.508	0.147	14.5	3.5
2	24.0		F	Baseline	0.647	0.144		8.6
2	24.6	32.9	F	Follow- up	0.683	0.141		4.9
3	25.0		F	Baseline	0.673	0.130	7.1	7.1
3	25.6	30.6	F	Follow- up	0.761	0.134	5.8	21.3
4	26.0		F	Baseline	0.713	0.136	13.4	6.0
4	26.6	33.0	F	Follow- up	0.762	0.152	14.2	4.9
5	28.0		M	Baseline	0.685	0.188	5.3	6.8
5	28.6	32.0	M	Follow- up	0.732	0.183	10.2	8.4
6	29.0		M	Baseline	0.544	0.166	4.8	4.9
6	29.6	30.6	M	Follow- up	0.538	0.152	2.4	5.6
7	32.0		M	Baseline	0.602	0.168	11.2	9.3
7	32.6	32.0	M	Follow- up	0.729	0.173	6.5	12.5
8	34.0		F	Baseline	0.492	0.113	21.7	4.0
8	34.6	31.6	F	Follow- up	0.426	0.118	1.2	4.2
9	37.0		M	Baseline	0.348	0.152	5.1	12.7
9	37.6	32.7	M	Follow- up	0.556	0.154	5.4	6.6
10	38.0		M	Baseline	0.595	0.113	4.7	9.0
10	38.6	33.0	M	Follow- up	0.726	0.117	5.3	10.6
11	41.0		M	Baseline	0.531	0.056		4.7
11	41.6	33.0	M	Follow- up	0.554	0.039		21.3
12	53.0		F	Baseline	1.117	0.159	14.8	17.7
12	53.6	32.0	F	Follow- up	1.067	0.149	17.5	14.3
13	53.0		F	Baseline	0.811	0.153	24.2	12.9
13	53.6	32.6	F	Follow- up	0.544	0.178	24.0	12.9
14	56.0		F	Baseline	0.624	0.147	9.9	4.1
14	56.6	32.0	F	Follow- up	0.713	0.143	9.1	21.1
15	57.0		F	Baseline	0.904	0.149	4.8	6.1
15	57.6	30.6	F	Follow- up	0.781	0.149	7.2	9.8
16	57.0		M	Baseline	0.875	0.116	17.2	13.6
16	57.6	32.7	M	Follow- up	0.637	0.111	11.3	13.1
17	58.0		F	Baseline	0.621	0.125	2.3	4.7
17	58.6	32.7	F	Follow- up	0.596	0.114	2.3	7.8
18	60.0		M	Baseline	0.650	0.181	9.6	2.7
18	60.6	32.7	M	Follow- up	0.807	0.156	3.7	14.1
19	60.0		M	Baseline	0.914	0.133	17.6	9.1
19	60.6	30.6	M	Follow- up	0.674	0.137	4.0	7.6
20	60.6	30.6	M	Baseline	0.249	0.164	7.3	11.1
20	60.0		M	Follow- up	0.375	0.166	6.6	27.0
21	63.0		F	Baseline	0.713	0.122	12.8	12.5
21	63.6	33.0	F	Follow- up	0.957	0.124	13.7	18.5
22	64.0		F	Baseline	0.516	0.148	7.2	15.7
22	64.6	33.0	F	Follow- up	0.390	0.164	5.0	17.1
23	68.0		F	Baseline	0.476	0.132	15.8	24.9
23	68.6	33.0	F	Follow- up	0.711	0.151	17.7	24.2

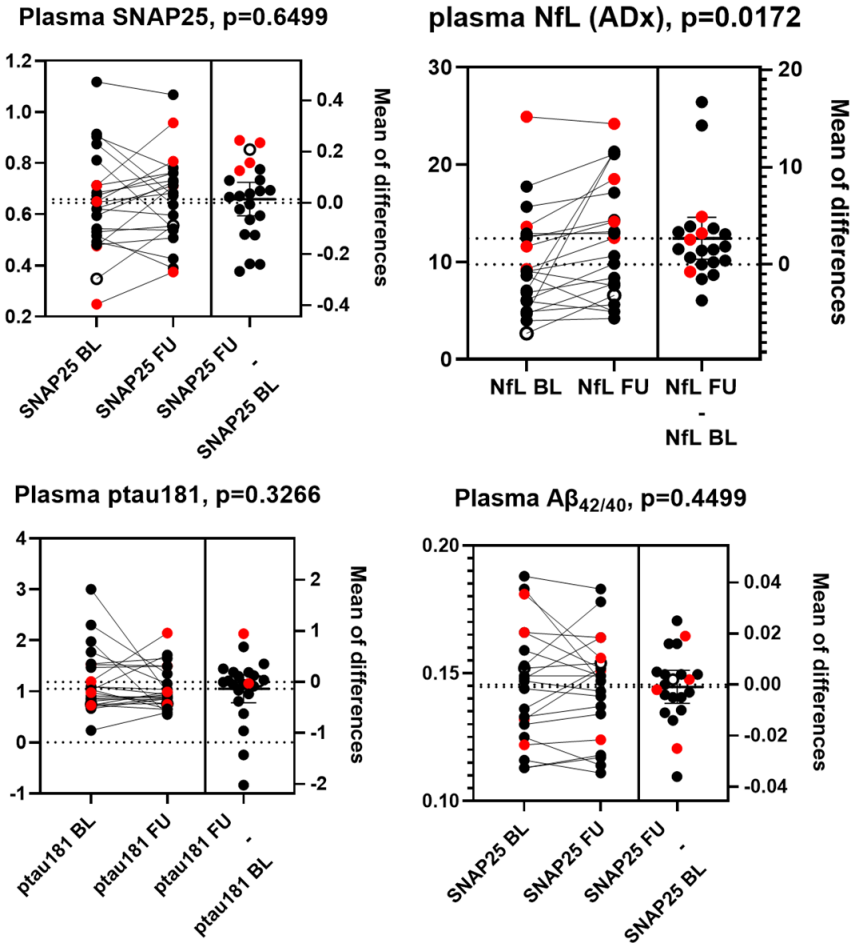

Figure 1: Plasma biomarkers levels at baseline and follow-up (33 weeks, 7 months) and p-value for the paired analysis. The right- hand side represents the group- differences from baseline to follow-up, while the left- hand side represents the age-dependent increase in plasma biomarkers. The individuals marked in red were the oldest individuals among these volunteers, while the open circles also had increased SNAP25 levels after follow-up, but is 37 years young.

REFERENCES
(1) Thijssen EH et al., DOI: 10.1038/s41598-021-89004-x.
(2) Bayoumy S et al., DOI: 10.1186/s13195-021-00939-9.

CONTACT
eugeen.vanmechelen@adxneurosciences.com