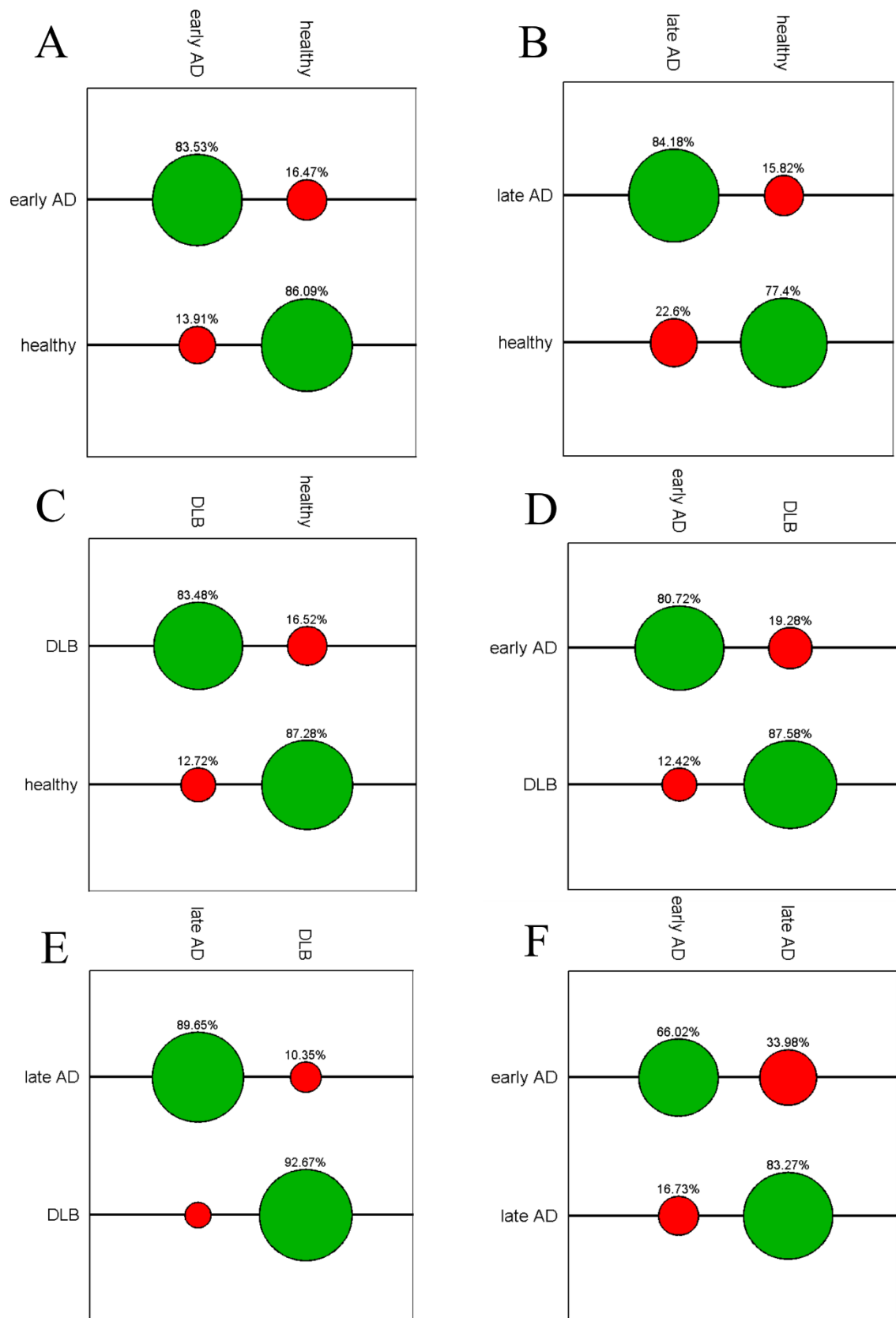


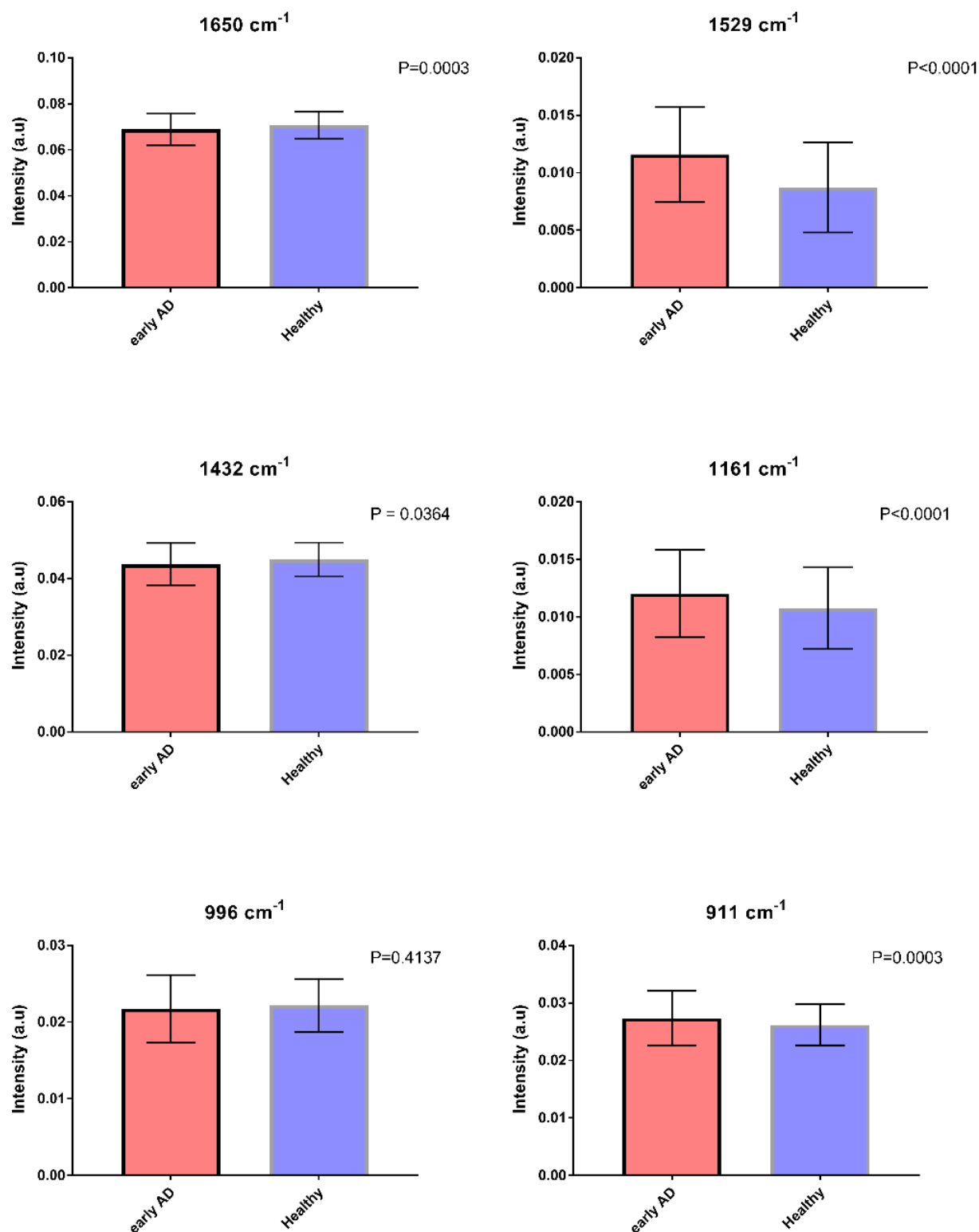
Supplementary Information

Raman spectroscopy to diagnose Alzheimer's disease and dementia with Lewy bodies in blood

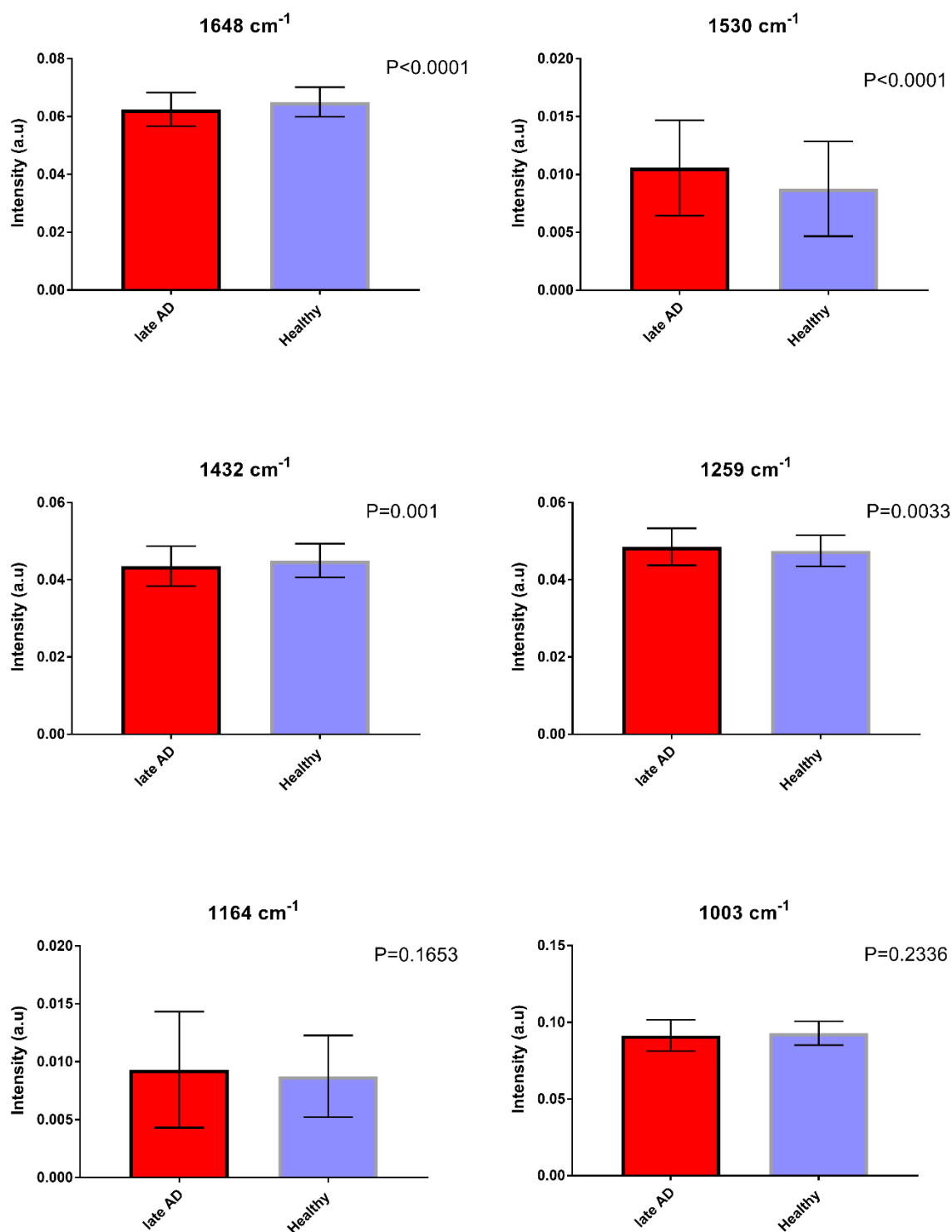
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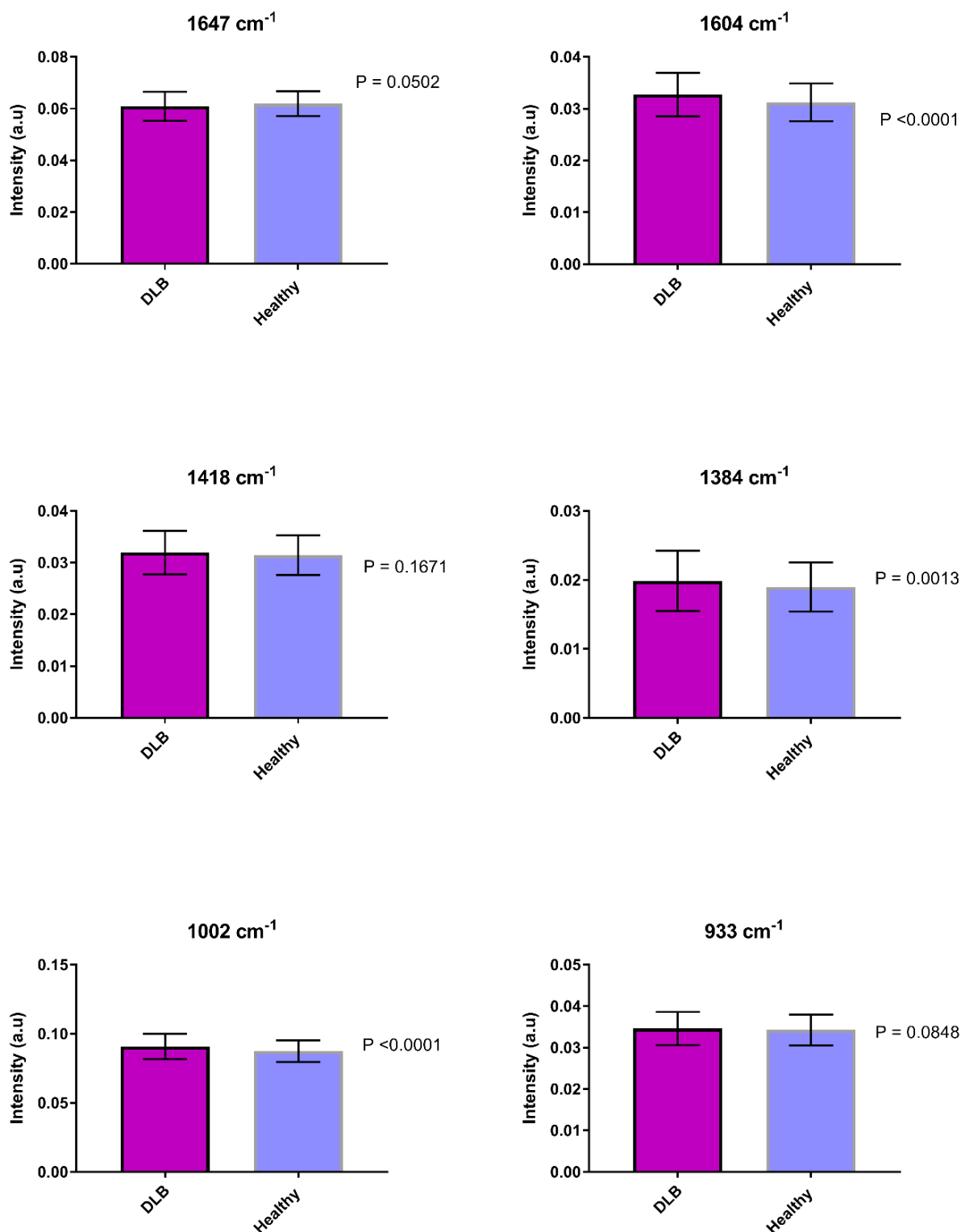
Supplementary Figure 1. Sensitivity and specificity rates after classification with support vector machine (SVM). Early-stage Alzheimer's disease (AD) *versus* healthy individuals (A); late-stage AD *versus* healthy individuals (B); dementia with Lewy bodies (DLB) *versus* healthy individuals (C); early-stage AD *versus* DLB (D); late-stage AD *versus* DLB (E); early-stage AD *versus* late-stage AD (F).



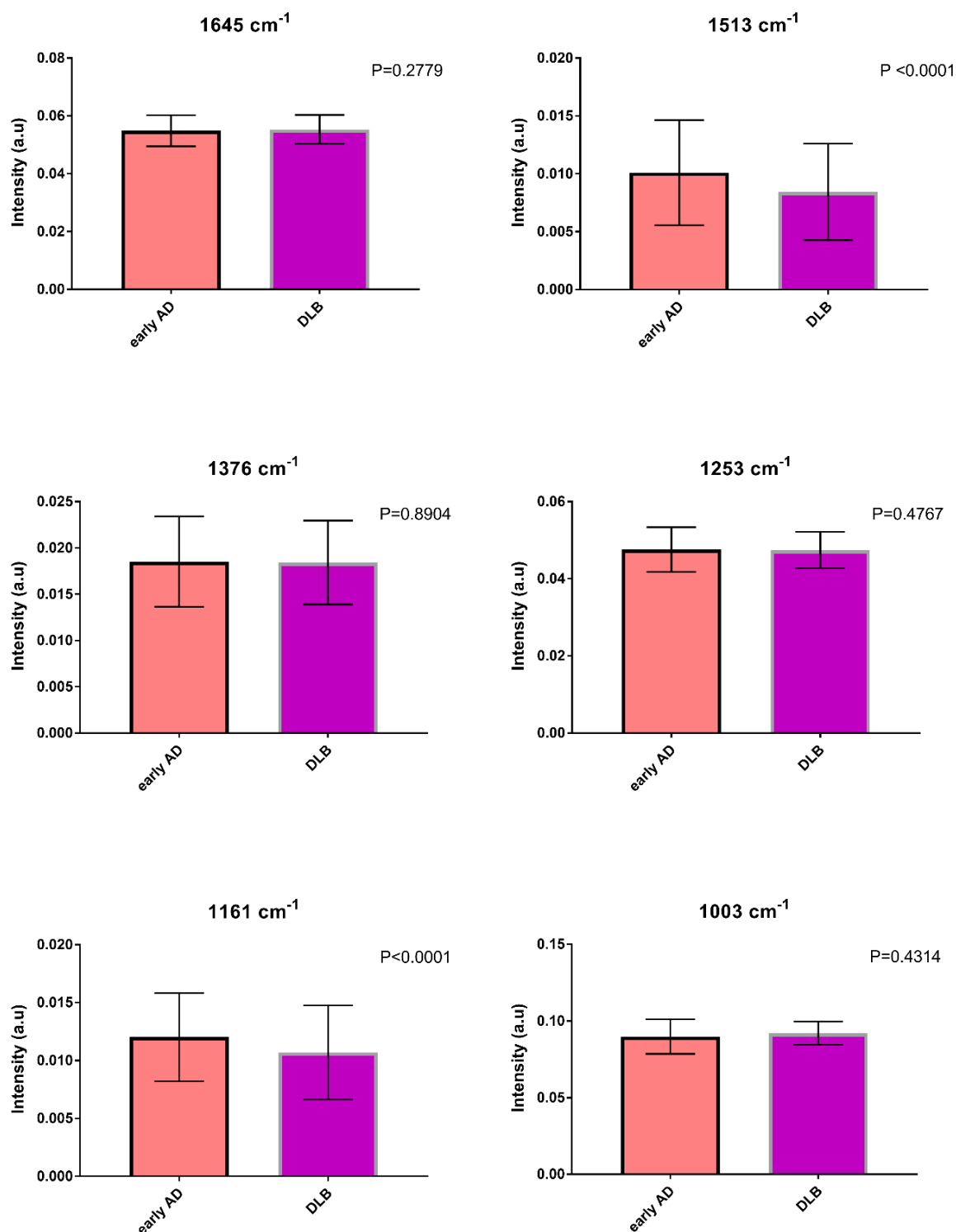
Supplementary Figure 2. Differences in the intensity levels of important biomolecules after the comparison between early-stage AD and healthy individuals. Tentative assignments for the above wavenumbers are: 1650 cm^{-1} (Amide I, proteins), 1529 cm^{-1} (Amide II, proteins), 1432 cm^{-1} (CH_2 vibrations of lipids), 1161 cm^{-1} (vibrations of quinoid ring), 996 cm^{-1} (nucleic acid) and 911 cm^{-1} (glucose) [1, 2]. Data are expressed as the mean \pm standard deviation (SD) (see Supplementary Table 1).



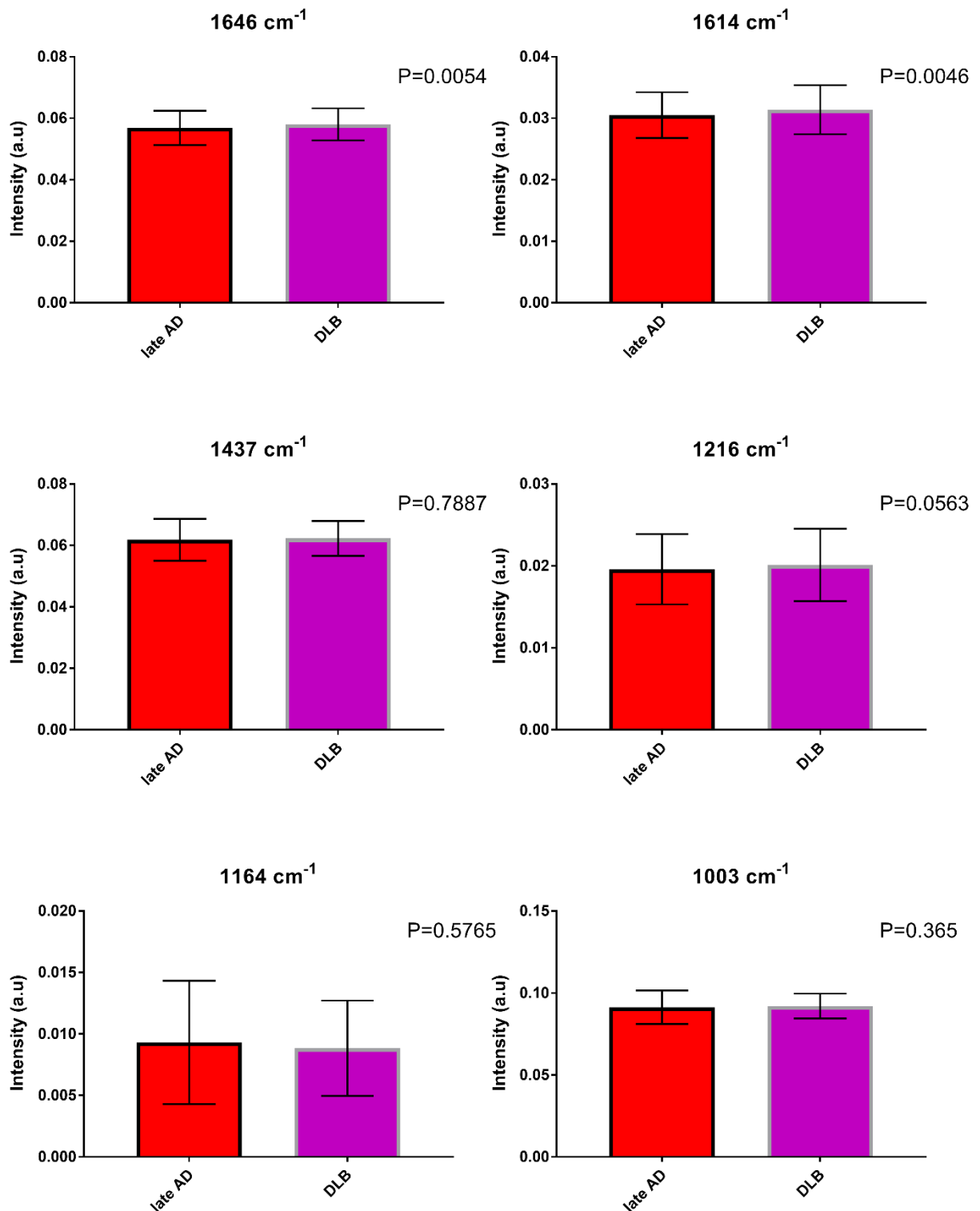
Supplementary Figure 3. Differences in the intensity levels of important biomolecules after the comparison between late-stage AD and healthy individuals. Tentative assignments for the above wavenumbers are: 1648 cm^{-1} (Amide I, proteins), 1530 cm^{-1} (Amide II, proteins), 1432 cm^{-1} (CH_2 vibrations of lipids), 1259 cm^{-1} (Amide III, proteins), 1164 cm^{-1} (carbohydrates) and 1003 cm^{-1} (phenylalanine) [1, 2]. Data are expressed as the mean \pm standard deviation (SD) (See Supplementary Table 1).



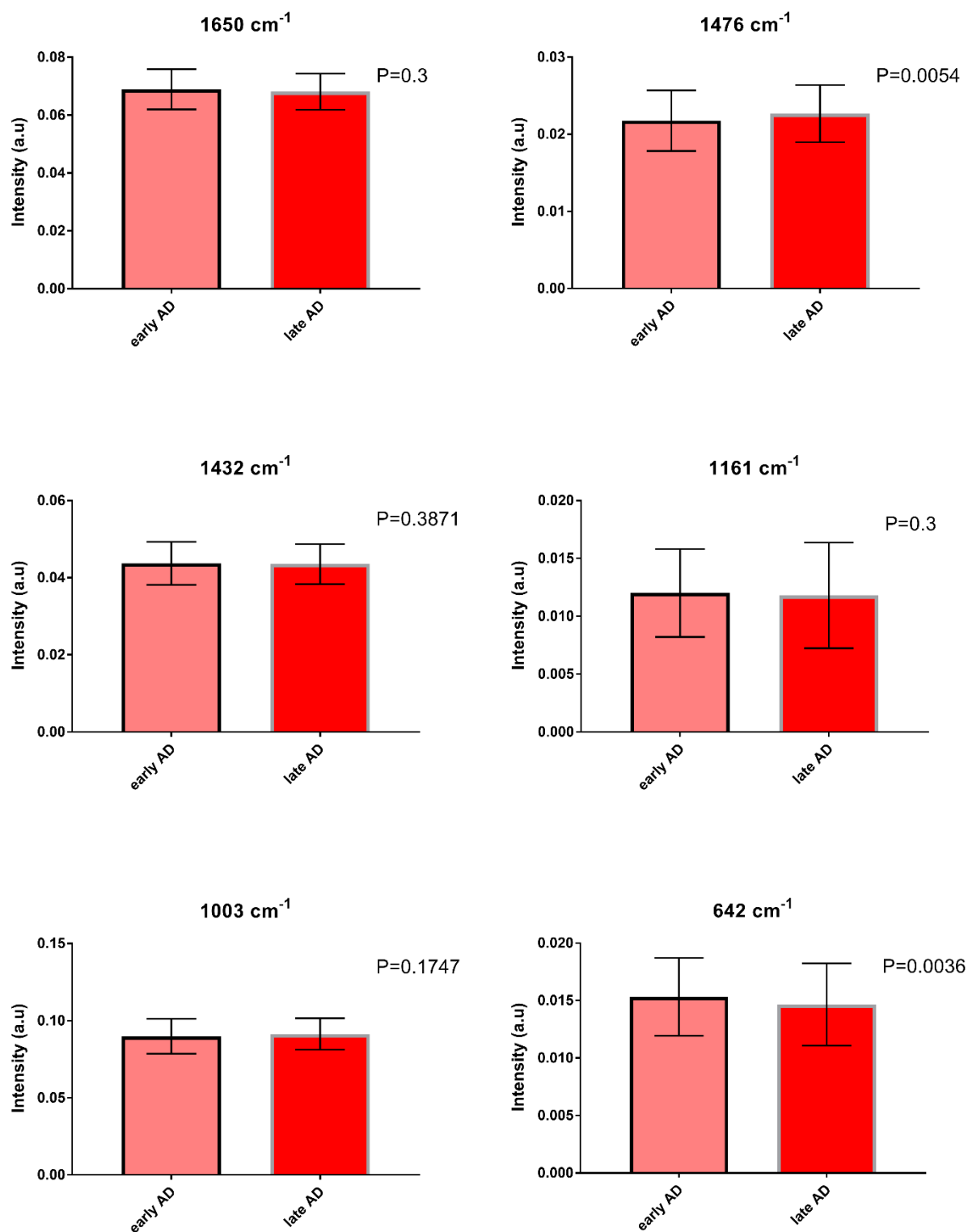
Supplementary Figure 4. Differences in the intensity levels of important biomolecules after the comparison between DLB and healthy individuals. Tentative assignments for the above wavenumbers are: 1674 cm^{-1} (Amide I, proteins), 1604 cm^{-1} (Amide I, proteins), 1418 cm^{-1} (C=C stretching of quinoid ring), 1384 cm^{-1} (CH_3 vibration of lipids), 1002 cm^{-1} (phenylalanine), 933 cm^{-1} (collagen) [1, 2]. Data are expressed as the mean \pm standard deviation (SD) (See Supplementary Table 1).



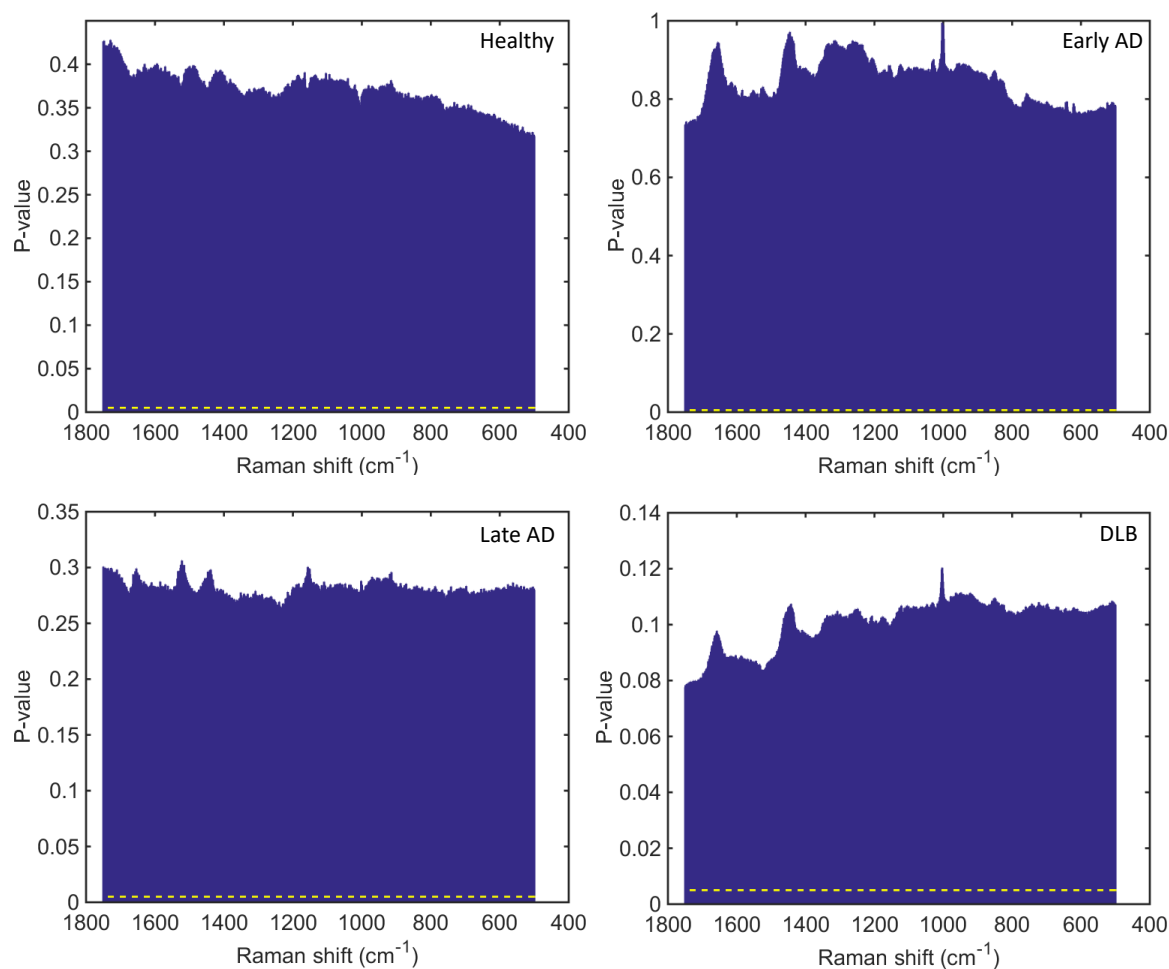
Supplementary Figure 5. Differences in the intensity levels of important biomolecules after the comparison between early-stage AD and DLB. Tentative assignments for the above wavenumbers are: 1645 cm^{-1} (Amide I, proteins), 1513 cm^{-1} (Amide II, proteins), 1376 cm^{-1} (CH_3 , lipids), 1253 cm^{-1} (Amide III, proteins), 1161 cm^{-1} (vibrations of quinoid ring) and 1003 cm^{-1} (phenylalanine) [1, 2]. Data are expressed as the mean \pm standard deviation (SD) (See Supplementary Table 1).



Supplementary Figure 6. Differences in the intensity levels of important biomolecules after the comparison between late-stage AD and DLB. Tentative assignments for the above wavenumbers are: 1646 cm^{-1} (Amide I, proteins), 1614 cm^{-1} (Amide I, proteins), 1437 cm^{-1} (CH_2 vibrations of lipids), 1216 cm^{-1} (Amide III, proteins), 1164 cm^{-1} (carbohydrates) and 1003 cm^{-1} (phenylalanine) [1, 2]. Data are expressed as the mean \pm standard deviation (SD) (See Supplementary Table 1).



Supplementary Figure 7. Differences in the intensity levels of important biomolecules after the comparison between early-stage AD and late-stage AD. Tentative assignments for the above wavenumbers are: 1650 cm^{-1} (Amide I, proteins), 1476 cm^{-1} (Amide II, proteins), 1432 cm^{-1} (CH_3 , lipids), 1161 cm^{-1} (vibrations of quinoid ring), 1003 cm^{-1} (phenylalanine) and 642 cm^{-1} (C-C and C-S vibrations of proteins) [1, 2]. Data are expressed as the mean \pm standard deviation (SD) (See Supplementary Table 1).



Supplementary Figure 8. P-values calculated for gender comparison ('Male' versus 'Female') based on their Raman spectra. Two-tail p-value calculated for each wavenumber in a 95% confidence level, where AD stands for Alzheimer's disease and DLB stands for dementia with Lewy bodies. Dashed yellow line marks the P-value of 0.005.

Supplementary Table 1. P-values (two-tail, 95% confidence level) for the different ages in each comparison group.

Comparison Group	P-value
Early AD vs Healthy	0.106
Late AD vs Healthy	0.004
DLB vs Healthy	< 0.001
Early AD vs DLB	0.026
Late AD vs DLB	0.213
Early AD vs Late AD	0.277

AD: Alzheimer's disease; DLB: dementia with Lewy bodies

Supplementary Table 2. Mean values, standard deviations (SD), 95% confidence intervals (CI) and P-values after statistical analysis for the different comparison groups.

Early-stage AD vs HC				
Wavenumber (cm ⁻¹)	Early AD	Healthy	95% CI	P-value
	Means/SD			
1650	0.0689/0.0069	0.0707/0.0059	0.0008 to 0.0028	0.0003
1529	0.0116/0.0041	0.0087/0.0039	-0.0034 to -0.0022	<0.0001
1432	0.0437/0.0059	0.0449/0.0044	0.00004 to 0.0015	0.0364
1161	0.012/0.0038	0.0107/0.0035	-0.0019 to -0.0007	<0.0001
996	0.0217/0.0044	0.0222/0.0035	-0.0003 to 0.0008	0.4137
911	0.0273/0.0048	0.0262/0.0036	-0.0018 to -0.0006	0.0003
Late-stage AD vs HC				
Wavenumber (cm ⁻¹)	Late AD	Healthy	95% CI	P-value
	Means/SD			
1648	0.0625/0.0058	0.065/0.0051	0.0016 to 0.0029	<0.0001
1530	0.1057/0.0042	0.0087/0.0041	-0.0024 to -0.0013	<0.0001
1432	0.0435/0.0052	0.0449/0.0044	0.0004 to 0.0016	0.001
1259	0.0485/0.0048	0.0475/0.004	-0.0014 to -0.0003	0.0033
1164	0.0093/0.005	0.0087/0.0035	-0.0009 to 0.0002	0.1653
1003	0.0913/0.0102	0.0928/0.0078	-0.0003 to 0.0014	0.2336

DLB vs HC				
Wavenumber (cm⁻¹)	DLB	Healthy	95% CI	P-value
	Means/SD			
1647	0.0609/0.0056	0.0619/0.0048	0 to 0.0014	0.0502
1604	0.0328/0.0042	0.0312/0.0036	-0.0021 to -0.001	<0.0001
1418	0.0319/0.0042	0.0314/0.0038	-0.0009 to 0.0002	0.1671
1384	0.0199/0.0043	0.0189/0.0036	-0.0015 to -0.0004	0.0013
1002	0.0908/0.0092	0.0874/0.0079	-0.0043 to -0.0023	<0.0001
933	0.0346/0.004	0.0343/0.0037	-0.001 to 0.0001	0.0848
Early-stage AD vs DLB				
Wavenumber (cm⁻¹)	Early AD	DLB	95% CI	P-value
	Means/SD			
1645	0.0549/0.0054	0.0553/0.0049	-0.0003 to 0.0013	0.2779
1513	0.0101/0.0045	0.0084/0.0042	-0.0024 to -0.0011	<0.0001
1376	0.0185/0.0049	0.0184/0.0045	-0.0007 to 0.0007	0.8904
1253	0.0476/0.0058	0.0474/0.0047	-0.0005 to 0.001	0.4767
1161	0.012/0.0038	0.0107/0.0041	-0.002 to -0.0008	<0.0001
1003	0.0898/0.0113	0.0919/0.0075	-0.0007 to 0.0017	0.4314

Late-stage AD vs DLB				
Wavenumber (cm ⁻¹)	Late AD	DLB	95% CI	P-value
	Means/SD			
1646	0.0568/0.0056	0.058/0.0052	0.0003 to 0.0016	0.0054
1614	0.0305/0.0037	0.0314/0.0039	0.0002 to 0.0013	0.0046
1437	0.0618/0.0068	0.0623/0.0057	-0.0007 to 0.0009	0.7887
1216	0.0196/0.0043	0.0201/0.0044	-0.0006 to 0.0012	0.0563
1164	0.0093/0.005	0.0088/0.0038	-0.0007 to 0.0004	0.5765
1003	0.0913/0.0102	0.0919/0.0076	-0.0014 to 0.0005	0.365
Early-stage AD vs late-stage AD				
Wavenumber (cm ⁻¹)	Early AD	Late AD	95% CI	P-value
	Means/SD			
1650	0.0689/0.0069	0.0681/0.0063	-0.0015 to 0.0005	0.3
1476	0.0218/0.0039	0.0227/0.0037	0.0002 to 0.0014	0.0054
1432	0.0437/0.0056	0.0435/0.0052	-0.001 to 0.0004	0.3871
1161	0.012/0.0038	0.0118/0.0046	-0.0009 to 0.0003	0.3
1003	0.0898/0.0113	0.0913/0.0102	-0.0003 to 0.0019	0.1747
642	0.0153/0.0034	0.0147/0.0036	-0.0013 to -0.0003	0.0036

Abbreviations: AD = Alzheimer's disease; HC = healthy controls; DLB = dementia with Lewy bodies; SD = standard deviation; CI = confidence interval

References

- [1] Movasaghi Z, Rehman S, Rehman IU. Raman spectroscopy of biological tissues. *Applied Spectroscopy Reviews*. 2007;42:493-541.
- [2] Pichardo-Molina JL, Frausto-Reyes C, Barbosa-García O, Huerta-Franco R, González-Trujillo JL, Ramírez-Alvarado CA, et al. Raman spectroscopy and multivariate analysis of serum samples from breast cancer patients. *Lasers in Medical Science*. 2007;22:229-36.