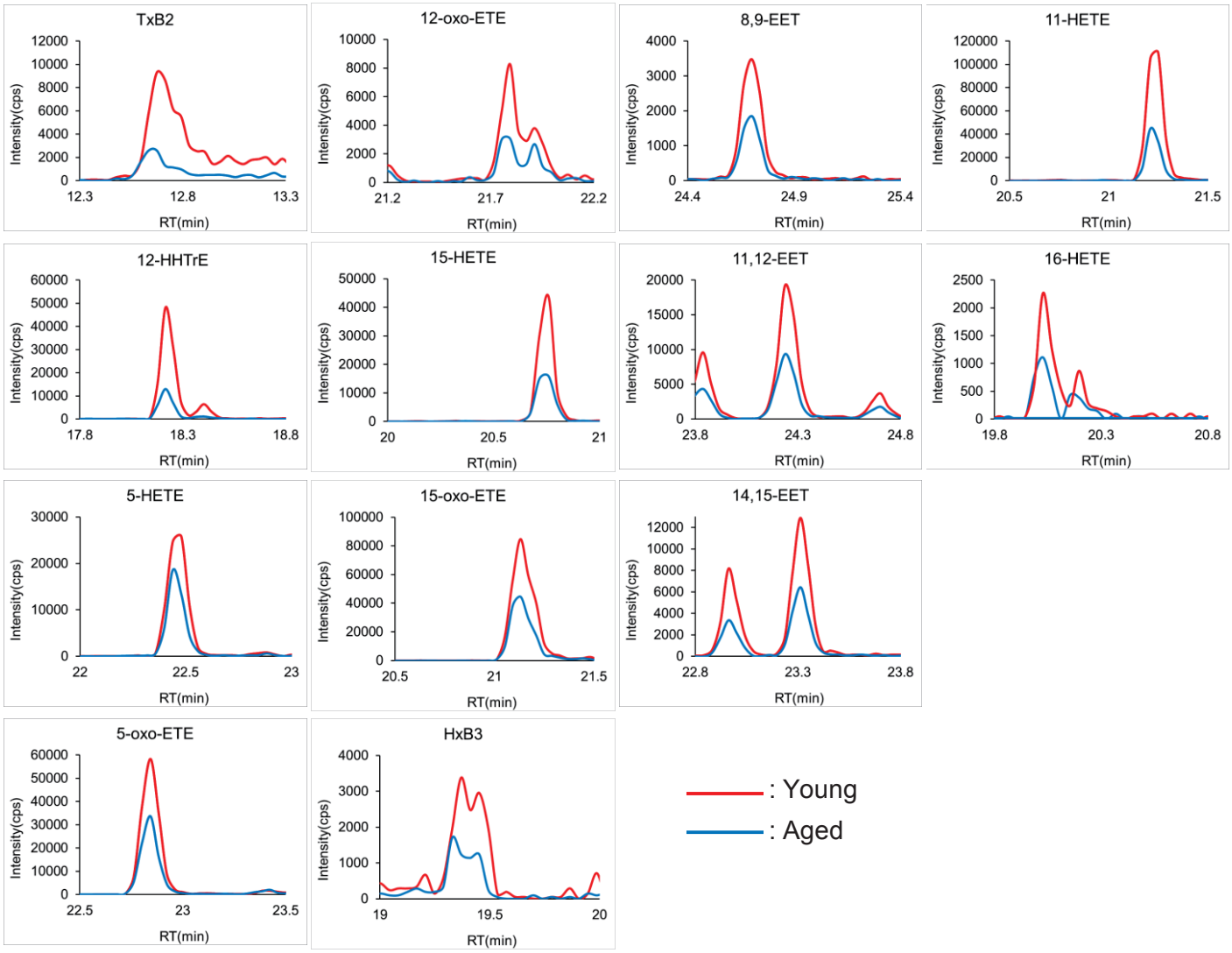
Supplement Figure 1



Age-related changes in the typical LC-MS/MS chromatograms of ARA-derived metabolites. Data shows a representative chromatogram of each metabolite in the hippocampus of the young (red line) and the aged mouse (blue line).

Supplement Table 1

Free FA	Oxylipin	
PA	LA [8]	
POA	5-LO	9-HODE
SA		9-oxo-ODE
OA	12/15-LO	13-HODE
LA		13-oxo-ODE
ALA	P450	9,10-EpOME
GLA		9,10-diHOME
SDA		12,13-EpOME
DGLA		12,13-diHOME
MA		
ETA	ALA [3]	
ARA	5-LO	9-HOTrE(n3)
EPA		9-oxo-OTrE(n3)
AdA	12/15-LO	13-HOTrE(n3)
DPA(n3)		
DPA(n6)	GLA [1]	
DHA	12/15-LO	13-HOTrE(n6)
	DGLA [6]	
	COX	PGE_1
		PGD_1
		PGF_{1a}
		TXB_1
	12/15-LO	15-HETrE(n6)
	(non-Enzyme)	8-HETrE(n6)
	DPA(n3) [1]	
	12/15-LO	17-HDoPE(n3)
	DPA(n6) [1]	
	12/15-LO	17-HDoPE(n6)
	MA [2]	
	5-LO	LTB_3
		5-HETrE(n9)

ARA [38]	
COX	PGE2
	PGD2
	15-keto-PGE2
	15-deoxy-PGJ2
	PGF2a
	6-keto-PGF1a
	TXB2
	12-HHTrE
5-LO	LTB4
	LTB4-20OH
	LTD4
	5-HETE
	5-oxo-ETE
12/15-LO	HxA3
	HxB3
	12-HETE
	12-oxo-ETE
	15-HETE
	15-oxo-ETE
	LXA4
	LXB4
	5,15-diHETE
	8,15-diHETE
P450	5,6-DHT
	8,9-EET
	8,9-DHT
	11,12-EET
	11,12-DHT
	14,15-EET
	14,15-DHT
(non-Enzyme)	8-HETE
	9-HETE
	11-HETE
	16-HETE
	17-HETE
	18-HETE
	19-HETE
	20-HETE

EPA [31]	
COX	PGE_3
	PGD_3
	$PGF_{3\alpha}$
	6-keto-PGF1α-$\measuredangle$17
	TXB_3
5-LO	LTB_5
	5-HEPE
12/15-LO	12-HEPE
	15-HEPE
	LXA_5
P450	8,9-EpETE
	8,9-diHETE
	11,12-EpETE
	11,12-diHETE
	14,15-EpETE
	14,15-diHETE
	17,18-EpETE
	17,18-diHETE
	12hy-17,18-EpETE
(non-Enzyme)	18-HEPE
	RvE_1
	RvE_2
	RvE_3
	8,18-diHEPE
	11,18-diHEPE
	12,18-diHEPE
	8-HEPE
	9-HEPE
	11-HEPE
	19-HEPE
	20-HEPE

DHA [30]	
COX	13-HDoHE
5-LO	10-HDoHE
12/15-LO	14-HDoHE
	4,14-diHDoHE
	7,14-diHDoHE
	17-HDoHE
	RvD_1
	RvD_2
	7-oxo-DoHE
	7,17-diHDoHE
	10,17-diHDoHE
P450	7,8-EpDPE
	7,8-diHDoPE
	10,11-EpDPE
	10,11-diHDoPE
	13,14-EpDPE
	13,14-diHDoPE
	16,17-EpDPE
	16,17-diHDoPE
	19,20-EpDPE
	19,20-diHDoPE
(non-Enzyme)	4-HDoHE
	7-HDoHE
	8-HDoHE
	11-HDoHE
	16-HDoHE
	21-HDoHE
	22-HDoHE
	20-HDoHE
	14,20-diHDoHE

Supplement Table 2

		Coxtex						Hippocampus						
		Young			Aged			Young			Aged			
	pg / mg tissue	Mean	±	SE	Mean	±	SE	Mean	±	SE	Mean	±	SE	
ARA														
(Enzyme)														
COX	PGE_2	1.2	±	0.3	1.1	±	0.5	1.2	±	0.3	0.6	±	0.2	
	PGD_2	24.3	±	3.4	18.5	±	5.7	25.7	±	4.4	14.9	±	2.7	
	15-keto-PGE_2		ND			ND			ND			ND		
	15-deoxy-PGJ_2		ND			ND			ND			ND		
	$PGF_{2\alpha}$	1.3	±	0.2	1.0	±	0.3	1.7	±	0.3	1.0	±	0.2	
	6-keto-PGF_{1a}		ND			ND			ND			ND		
	TXB_2	1.1	±	0.1	0.9	±	0.3	1.9	±	0.3	0.7	±	0.2	*
	12-HHTrE	14.8	±	1.8	12.4	±	3.6	21.6	±	3.3	12.9	±	1.9	*
5-LO	LTB_4		ND			ND			ND			ND		
	LTB_4-20OH		ND			ND			ND			ND		
	LTD_4		ND			ND			ND			ND		
	5-HETE	11.2	±	1.0	10.4	±	1.0	15.9	±	1.0	11.7	±	0.8	*
	5-oxo-ETE	11.3	±	0.8	10.9	±	0.9	13.4	±	0.9	9.6	±	0.7	*
12/15-LO	12-HETE	12.8	±	0.7	11.7	±	1.3	13.6	±	1.1	10.4	±	0.9	
	12-oxo-ETE	28.9	±	1.8	26.2	±	2.4	18.4	±	2.1	10.4	±	1.3	*
	15-HETE	20.7	±	1.3	20.6	±	2.8	25.0	±	1.7	17.2	±	1.6	*
	15-oxo-ETE	104.6	±	6.0	96.3	±	10.0	69.1	±	7.6	44.1	±	4.5	*
	HxA3		ND			ND			ND			ND		
	HxB3	12.0	±	1.0	10.6	±	1.3	17.1	±	1.9	9.9	±	2.2	*
	LXA4		ND			ND			ND			ND		
	LXB4		ND			ND			ND			ND		
	5,15-diHETE		ND			ND			ND			ND		
	8,15-diHETE		ND			ND			ND			ND		
P450	5,6-DHT		ND			ND			ND			ND		
	8,9-EET	3.0	±	0.5	1.5	±	0.7	4.0	±	0.6	1.0	±	0.6	*
	8,9-DHT		ND			ND			ND			ND		
	11,12-EET	4.2	±	0.3	3.4	±	0.3	5.2	±	0.5	3.1	±	0.3	*
	11,12-DHT		ND			ND			ND			ND		
	14,15-EET	7.7	±	0.8	6.1	±	0.5	8.3	±	0.9	4.5	±	0.5	*
	14,15-DHT		ND			ND			ND			ND		
(non-Enzyme)	8-HETE	5.6	±	0.4	5.4	±	0.6	6.8	±	0.8	4.4	±	0.4	
	9-HETE	8.2	±	0.7	7.1	±	0.9	10.9	±	0.8	7.1	±	0.5	
	11-HETE	9.9	±	1.0	8.7	±	1.5	11.6	±	1.0	7.3	±	0.7	*
	16-HETE	1.8	±	0.2	1.6	±	0.2	1.8	±	0.1	1.0	±	0.2	*
	17-HETE		ND			ND			ND			ND		
	18-HETE		ND			ND			ND			ND		
	19-HETE		ND			ND			ND			ND		
	20-HETE		ND			ND			ND			ND		

Age-related changes in the levels of metabolites derived from ARA in the cortex and hippocampus. Data are presented as the mean ± standard error (Cortex; young mice (n = 8), aged mice (n = 7), Hippocampus; young mice (n = 8), aged mice (n = 6)). There was a significant difference between the young and aged mice ($P < 0.05$, *Mann-Whitney test). COX, cyclooxygenase; LO, lipoxygenase; CYP, cytochrome P450

Supplement Table 3

		Coxtex				Hippocampus			
		Young		Aged		Young		Aged	
	pg / mg tissue	Mean ± SE		Mean ± SE		Mean ± SE		Mean ± SE	
LA									
(Enzyme)									
5-LO	9-HODE	4.7 ± 0.8		4.9 ± 0.8		4.7 ± 0.4		3.6 ± 0.4	
	9-oxo-ODE	ND		0.3 ± 0.3		ND		ND	
12/15-LO	13-HODE	12.3 ± 1.6		12.0 ± 1.4		11.6 ± 1.2		9.7 ± 1.1	
	13-oxo-ODE	1.2 ± 0.1		1.4 ± 0.3		0.5 ± 0.2		0.2 ± 0.2	
P450	9,10-EpOME	1.0 ± 0.2		0.8 ± 0.2		1.3 ± 0.2		1.0 ± 0.4	
	9,10-diHOME	0.7 ± 0.1		0.7 ± 0.0		0.6 ± 0.0		0.6 ± 0.1	
	12,13-EpOME	0.3 ± 0.2		0.3 ± 0.2		0.7 ± 0.2		0.5 ± 0.3	
	12,13-diHOME	ND		ND		ND		ND	
ALA									
5-LO	9-HOTrE(n3)	ND		ND		ND		ND	
	9-oxo-OTrE(n3)	ND		ND		ND		ND	
12/15-LO	13-HOTrE(n3)	ND		ND		ND		ND	
GLA									
12/15-LO	13-HOTrE(n6)	5.7 ± 0.6		4.9 ± 0.8		5.3 ± 0.5		5.9 ± 1.5	
DGLA									
COX	PGE_1	ND		0.3 ± 0.3		1.2 ± 0.3		0.5 ± 0.3	
	PGD_1	0.2 ± 0.0		0.1 ± 0.1		ND		ND	
	$PGF_{1\alpha}$	ND		ND		ND		ND	
	TXB_1	ND		ND		ND		ND	
12/15-LO	15-HETrE(n6)	0.5 ± 0.1		0.3 ± 0.1		0.4 ± 0.2		ND	
(non-Enzyme)	8-HETrE(n6)	ND		ND		ND		ND	
DPA(n3)									
12/15-LO	17-HDoPE(n3)	ND		ND		ND		ND	
DPA(n6)				ND				ND	
12/15-LO	17-HDoPE(n6)	ND		ND		ND		ND	
MA									
5-LO	LTB_3	ND		ND		ND		ND	
	5-HETrE(n9)	ND		ND		ND		ND	

		Coxtex				Hippocampus			
		Young		Aged		Young		Aged	
	pg / mg tissue	Mean ± SE		Mean ± SE		Mean ± SE		Mean ± SE	
EPA									
(Enzyme)									
COX	PGE_3	ND		ND		ND		ND	
	PGD_3	ND		ND		ND		ND	
	$PGF_{3\alpha}$	ND		ND		ND		ND	
	6-keto-PGF1α-⊿17	ND		ND		ND		ND	
	TXB_3	ND		ND		ND		ND	
5-LO	LTB_5	ND		ND		ND		ND	
	5-HEPE	ND		ND		ND		ND	
12/15-LO	12-HEPE	ND		ND		ND		ND	
	15-HEPE	ND		ND		ND		ND	
	LXA_5	ND		ND		ND		ND	
P450	8,9-EpETE	ND		ND		ND		ND	
	8,9-diHETE	ND		ND		ND		ND	
	11,12-EpETE	2.6 ± 0.2		1.4 ± 0.4		ND		ND	
	11,12-diHETE	ND		ND		ND		ND	
	14,15-EpETE	ND		ND		ND		ND	
	14,15-diHETE	ND		ND		ND		ND	
	17,18-EpETE	ND		ND		ND		ND	
	17,18-diHETE	ND		ND		ND		ND	
	12hy-17,18-EpETE	ND		ND		ND		ND	
(non-Enzyme)	18-HEPE	ND		ND		ND		ND	
	RvE_1	ND		ND		ND		ND	
	RvE_2	ND		ND		ND		ND	
	RvE_3	ND		ND		ND		ND	
	8,18-diHEPE	ND		ND		ND		ND	
	11,18-diHEPE	ND		ND		ND		ND	
	12,18-diHEPE	ND		ND		ND		ND	
	8-HEPE	ND		ND		ND		ND	
	9-HEPE	ND		ND		ND		ND	
	11-HEPE	ND		ND		ND		ND	
	19-HEPE	ND		ND		ND		ND	
	20-HEPE	ND		ND		ND		ND	
DHA									
(Enzyme)									
COX	13-HDoHE	0.6 ± 0.2		0.5 ± 0.2		0.8 ± 0.1		0.1 ± 0.1	*
5-LO	10-HDoHE	0.1 ± 0.1		ND		0.1 ± 0.1		ND	
12/15-LO	14-HDoHE	ND		ND		ND		ND	
	4,14-diHDoHE	ND		ND		ND		ND	
	7,14-diHDoHE	ND		ND		ND		ND	
	17-HDoHE	ND		ND		ND		ND	
	RvD_1	ND		ND		ND		ND	
	RvD_2	ND		ND		ND		ND	
	7-oxo-DoHE	ND		ND		ND		ND	
	7,17-diHDoHE	ND		ND		ND		ND	
	10,17-diHDoHE	ND		ND		ND		ND	
P450	7,8-EpDPE	ND		ND		ND		ND	
	7,8-diHDoPE	ND		ND		ND		ND	
	10,11-EpDPE	0.1 ± 0.1		ND		0.1 ± 0.1		ND	
	10,11-diHDoPE	ND		ND		ND		ND	
	13,14-EpDPE	ND		ND		ND		ND	
	13,14-diHDoPE	ND		ND		ND		ND	
	16,17-EpDPE	ND		ND		ND		ND	
	16,17-diHDoPE	ND		ND		ND		ND	
	19,20-EpDPE	ND		ND		ND		ND	
	19,20-diHDoPE	ND		ND		ND		ND	
(non-Enzyme)	4-HDoHE	0.7 ± 0.5		ND		2.2 ± 0.4		0.7 ± 0.5	
	7-HDoHE	ND		ND		ND		ND	
	8-HDoHE	0.7 ± 0.5		ND		0.9 ± 0.5		ND	
	11-HDoHE	0.4 ± 0.2		0.2 ± 0.2		0.4 ± 0.2		ND	
	16-HDoHE	0.9 ± 0.2		1.0 ± 0.1		1.0 ± 0.1		0.3 ± 0.2	*
	21-HDoHE	ND		ND		ND		ND	
	22-HDoHE	ND		ND		ND		ND	
	20-HDoHE	1.0 ± 0.5		0.8 ± 0.4		1.0 ± 0.4		0.5 ± 0.3	
	14,20-diHDoHE	ND		ND		0.1 ± 0.1		ND	

Age-related changes in the levels of metabolites derived from other PUFAs in the cortex and hippocampus. Data are presented as the mean ± standard error (Cortex; young mice (n = 8), aged mice (n = 7), Hippocampus; young mice (n = 8), aged mice (n = 6)). There was a significant difference between the young and aged mice ($P < 0.05$, *Mann-Whitney test). COX, cyclooxygenase; LO, lipoxygenase; CYP, cytochrome P450