^{1}H-NMR metabolomics reveals contrasting response by male and female mussels exposed to reduced seawater pH, increased temperature and a pathogen.

Robert P. Ellis, John I. Spicer, Jonathan J. Byrne, Ulf Sommer, Mark R. Viant, Daniel A. White and Steve Widdicombe

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Table S1 Metabolites in mantle tissue of *Mytilus edulis* identified as contributing over 50% to sex dissimilarity. Values are fold change in concentration of specific metabolites between males and females (mean ± SEM). % contribution indicates the contribution of each specific metabolite to the overall sex dissimilarity. Blue cells indicate metabolites that have a higher concentration in females, orange cells indicate a lower concentration in females. * unidentified metabolite at 1.10 ppm.

	Male:Female	
Metabolite	*Fold change*	*% cont.*
3-aminoisobutyric acid	1.58 ± 0.11	0.61
3-methylhistidine	2.38 ± 0.15	0.39
Adenisone monophosphate (AMP)	2.08 ± 0.11	2.22
Alanine	1.28 ± 0.09	5.24
Arginine	1.25 ± 0.06	1.98
Asparagine	1.28 ± 0.13	0.37
Aspartic acid	0.94 ± 0.12	1.13
Carnosine	1.17 ± 0.06	1.09
Dimethylamine	1.10 ± 0.14	0.34
Formic acid	0.42 ± 0.07	2.03
Glutamine	1.72 ± 0.08	1.88
Glycine	0.33 ± 0.02	2.39
Inosine monophosphate	0.77 ± 0.04	1.70
Isoleucine	1.08 ± 0.08	1.82
Leucine	1.23 ± 0.08	1.03
Lysine	0.50 ± 0.02	0.24
Proline	1.27 ± 0.07	0.58
Succinic acid	1.42 ± 0.10	0.49
Threonine	1.24 ± 0.08	1.88
Tyrosine	0.94 ± 0.11	1.93
Unidentified*	0.85 ± 0.05	3.23

Valine	0.90	±	0.05	3.74

Table S2 Metabolites in mantle tissue of *Mytilus edulis* identified as contributing over 50 % of group dissimilarity between mussels exposed to environmental stress. Values are fold change in concentration of specific metabolites between treatment groups (mean ± SEM). % contribution indicates the contribution of each specific metabolite to the overall group dissimilarity. Green cells indicate metabolites that have a higher concentration in exposure groups, red cells indicate a lower concentration in exposure groups. * unidentified metabolite at 1.10 ppm.

	Male								***Female***			
							Pre exposure & 1d post :					
	pH 8.05-7.35 : pH 6.50				**12.5°C : 17.0°C**		**7d post**		**pH 8.05-7.80 : pH 6.50**			
Metabolite	*Fold change*			*% cont.*	*Fold change*		*Fold change*		*Fold change*			*% cont.*
3-aminoisobutyric acid					0.68 ± 0.09		0.79 ± 0.08					
3-methylhistidine							0.97 ± 0.11		2.01 ± 0.35			0.33
Alanine	2.57 ± 0.78			2.24	0.77 ± 0.10		0.89 ± 0.09		1.03 ± 0.22			5.50
Adenosine monophosphate (AMP)					0.58 ± 0.12		1.36 ± 0.22		0.84 ± 0.18			1.74
Arginine					0.64 ± 0.08		0.94 ± 0.13		1.13 ± 0.20			4.69
Asparagine	3.13 ± 0.48			0.96	1.01 ± 0.09		0.92 ± 0.15		1.89 ± 0.31			1.18
Aspartic acid	0.89 ± 0.30			0.91	1.11 ± 0.25		0.86 ± 0.09		0.82 ± 0.15			1.92
Carnosine	0.37 ± 0.07			0.37	1.12 ± 0.10		1.10 ± 0.10					
Dimethylamine					1.15 ± 0.24		0.68 ± 0.10		0.98 ± 0.25			0.61
Formic acid	0.48 ± 0.23			1.60	1.08 ± 0.28		0.78 ± 0.16		0.22 ± 0.04			1.08

Glutamine	4.57	±	1.24	2.57	0.91	±	0.07	0.53	1.05	±	0.23	1.56	0.71	±	0.20	1.85
Glycine	0.32	±	0.10	2.88	1.08	±	0.16	2.34	0.38	±	0.04	2.63	1.74	±	0.50	0.58
Histidine													0.69	±	0.08	0.49
Inosine monophosphate	0.33	±	0.09	0.90	0.74	±	0.06	1.97	0.89	±	0.13	1.93	2.23		0.59	0.71
Isoleucine	6.32	±	1.70	7.68	0.49	±	0.05	2.59	0.80	±	0.15	2.74	1.53	±	0.38	2.04
Leucine	5.48	±	1.42	3.30	0.56	±	0.06	1.78	0.85	±	0.14	1.86	1.07	±	0.24	0.86
Lysine					1.08	±	0.12	0.35	0.72	±	0.09	0.28	0.95	±	0.28	1.34
Proline	3.83	±	1.71	0.47	0.97	±	0.11	0.35	1.09	±	0.09	0.32	3.24	±	1.59	5.07
Succinic acid	2.08	±	0.56	2.02	0.96	±	0.12	0.62	1.22	±	0.10	0.58	0.47	±	0.08	0.60
Taurine													0.61	±	0.11	0.66
Threonine	1.53	±	0.27	2.18	0.80	±	0.08	1.67	0.92	±	0.08	1.54	0.81		0.18	0.65
Tyrosine	5.83	±	1.04	5.69	0.89	±	0.13	2.11	0.90	±	0.14	2.25	2.14	±	0.50	2.17
Unidentified*					1.21	±	0.11	3.55	0.83	±	0.07	3.74	1.19	±	0.23	1.43
Valine	4.86	±	1.04	10.09	1.09	±	0.09	4.77	0.86	±	0.09	5.11	0.90	±	0.09	2.99

Table S3 Metabolites in mantle tissue of male *Mytilus edulis* identified as contributing over 50 % of group dissimilarity between treatment groups, as highlighted by the interaction of reduced seawater pH and a bacterial challenge. Values are mean fold change in concentration of specific metabolites between treatment groups (± SEM). % contribution indicates the contribution of each specific metabolite to the overall group dissimilarity. Green cells indicate metabolites that have a higher concentration in the exposure group, red cells indicate a lower concentration in exposure group. * unidentified metabolite at 1.10 ppm.

	Pre exposure						***1 d post exposure***	
	pH 8.05-7.35 : pH 6.50			**pH 8.05-7.80 : pH 7.35**			**pH 7.80 : pH 7.60 & 6.50**	
Metabolite	*Fold change*		*% cont.*	*Fold change*		*% cont.*	*Fold change*	*% cont.*
3-aminoisobutyric acid				0.93	± 0.15	1.83	0.09	2.03
Alanine	4.38	± 1.00	1.74	0.98	± 0.20	6.74	1.83	5.89
Adenosine monophosphate (AMP)				0.24	± 0.08	0.92	1.10	1.18
Arginine							1.76	0.48
Asparagine	5.87	± 1.66	0.99	1.19	± 0.24	0.75	5.52	0.35
Aspartic acid	5.24	± 0.79	0.42	1.21	± 0.23	0.32	0.14	0.31
Carnosine	4.83	± 1.32	0.93	1.19	± 0.36	1.25	1.11	0.70
Dimethylamine				1.76	± 0.23	0.31	1.32	0.30
Formic acid	0.26	± 0.05	1.53	0.77	± 0.14	2.19	0.09	3.08
Glutamine	1.46	± 0.51	1.54	0.98	0.20	5.34	13.40	0.96

Glycine	3.86	±	0.61	2.92	1.00	±	0.34	2.05	0.11	3.68
Inosine monophosphate	2.67	±	1.00	1.39	0.91	±	0.23	0.33	0.45	0.61
Isoleucine	3.47	±	1.64	8.99	1.01	±	0.19	2.65	7.59	3.16
Leucine	0.64	±	0.32	3.21	1.22	±	0.21	0.70	7.47	1.08
Lysine					1.49	±	0.20	0.67	1.79	0.43
Proline	0.31	±	0.08	0.47	1.48	±	0.30	1.00	2.03	0.47
Succinic acid	3.00	±	0.36	2.43	1.03	±	0.29	3.65	6.73	2.21
Threonine	3.73	±	1.31	2.28	0.63	±	0.06	0.43	8.62	2.41
Tyrosine	2.47	±	0.50	5.65	1.12	±	0.23	2.09	7.82	2.23
Unidentified*					1.35	±	0.17	4.85	0.74	3.87
Valine	0.32	±	0.05	9.07	0.94	±	0.12	3.52	6.02	3.64

Table S4 Number of deaths, and percentage mortality (in parentheses based on initial density of 24 mussels per treatment), within each treatment group over the initial 90-day experimental exposure. No additional mortality was noted following a bacterial exposure and therefore treatment groups are not separated by bacterial exposure group.

	Temperature (°C)	
pH	**12.5**	**17.0**
8.05	2 (8.33)	1 (4.16)
7.80	0 (0.00)	3 (12.50)
7.60	2 (8.33)	3 (12.50)
7.35	1 (4.16)	8 (33.33)
6.50	13 (45.83)	19 (79.17)