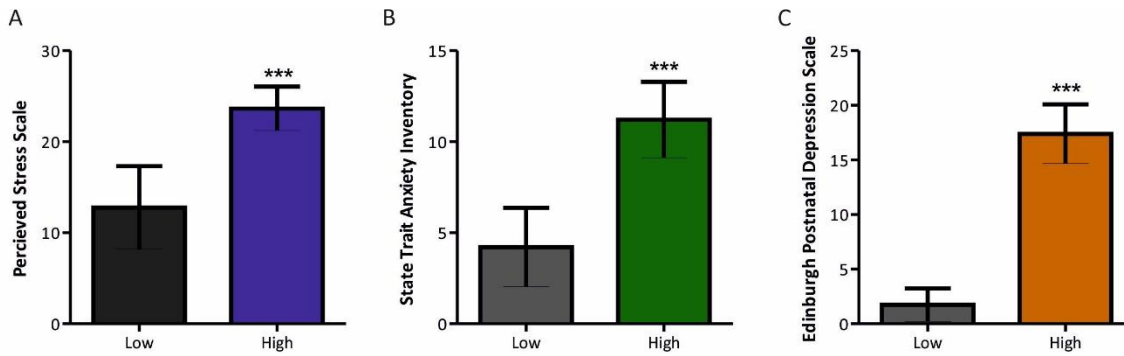


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Authors	Togher, Katie L.;Treacy, Eimear;O'Keeffe, Gerard W.;Kenny, Louise C.
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Supplementary Information

Supplementary figure 1: Participants groupings based on Questionnaire Scorings



Supplementary figure 1: Graphical representation of perceived stress scale (A), State Trait Anxiety Inventory (B) and Edinburgh Postnatal Depression Scale (C) scores between women ranked in the low and high categories. Unpaired student t-test show a significant difference between groups $P < 0.001$ ***, $N=121$.

Supplementary table 1: Global sample means of measured variables

<i>Measure</i>	<i>Population</i>	<i>Low</i>	<i>High</i>
	Mean $\pm$ SD (N)	Mean $\pm$ SD (N)	Mean $\pm$ SD (N)
Perceived Stress Scale	15.88 $\pm$ 6.5 (121)	12.75 $\pm$ 4.5 (81)	23.65 $\pm$ 2.4 (40)
State Trait Anxiety Inventory	6.17 $\pm$ 3.8 (121)	4.20 $\pm$ 2.1 (87)	11.21 $\pm$ 2.0 (34)
Edinburgh Postnatal Depression Scale	9.07 $\pm$ 5.6 (121)	6.52 $\pm$ 3.7 (90)	16.48 $\pm$ 2.9 (31)

Supplementary table 1: Global sample means of measured variables expressed as mean $\pm$ SD.

High stress (PSS $\geq$ 20), low stress (PSS $\leq$ 19). High anxiety (STAI $\geq$ 9), low anxiety (STAI $\leq$ 8).

High probability of depression (EPDS $\geq$ 13), low probability of depression (EPDS $\leq$ 12).

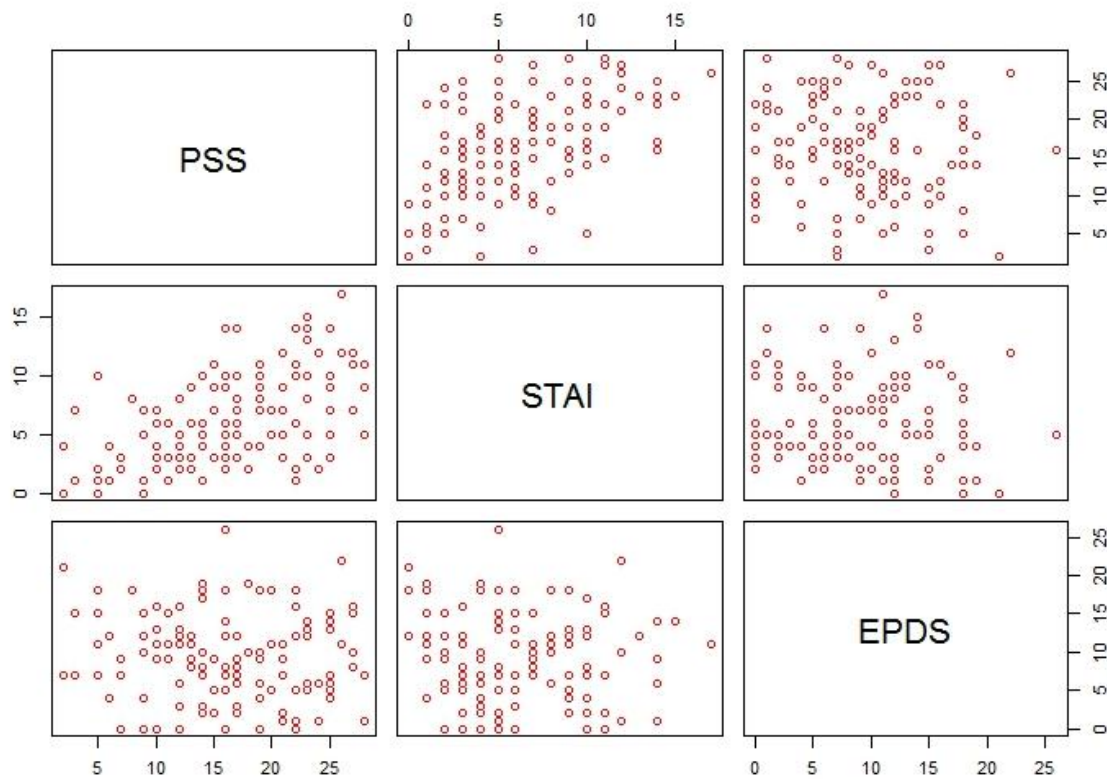
Supplementary table 2: Prenatal stress, anxiety and depression and other neonatal outcomes

<i>Perceived Stress Scale</i>		
	OR (CI ; <i>p</i> -value)	aOR (CI ; <i>p</i> -value)
Birth centiles	0.429 (0.115 – 1.606 ; 0.209)	0.395 (0.104 – 1.501 ; 0.173)
Neonatal Resuscitation	0.404 (0.109 – 1.501 ; 0.176)	0.460 (0.122 – 1.743 ; 0.253)
NICU Admission	1.405 (0.225 – 8.774 ; 0.716)	1.572 (0.240 – 10.312 ; 0.637)
<i>Stat Trait Anxiety Inventory</i>		
	OR (CI ; <i>p</i> -value)	aOR (CI ; <i>p</i> -value)
Birth centiles	1.279 (0.407 – 4.019 ; 0.673)	1.272 (0.396 – 4.080 ; 0.686)
Neonatal Resuscitation	1.142 (0.368 – 3.544 ; 0.818)	1.206 (0.375 – 3.873 ; 0.753)
NICU Admission	4.448 (0.708 – 27.954 ; 0.111)	1.109 (0.930 – 1.323 ; 0.250)
<i>Edinburgh Postnatal Depression Scale</i>		
	OR (CI ; <i>p</i> -value)	aOR (CI ; <i>p</i> -value)
Birth centiles	0.650 (0.172 – 2.456 ; 0.525)	0.602 (0.152 – 2.382 ; 0.469)
Neonatal Resuscitation	0.618 (0.164 – 2.324 ; 0.476)	0.654 (0.165 – 2.593 ; 0.546)
NICU Admission	2.071 (0.329 – 13.032 ; 0.438)	1.857 (0.277 – 12.460 ; 0.524)
<i>Cumulative</i>		
	OR (CI ; <i>p</i> -value)	aOR (CI ; <i>p</i> -value)
Birth centiles	0.363 (0.045 – 2.945 ; 0.342)	0.334 (0.039 – 2.855 ; 0.316)

Neonatal Resuscitation	0.764 (0.158 – 3.689 ; 0.738)	0.795 (0.158 – 4.003 ; 0.781)
NICU Admission	4.444 (0.685 – 28.828 ; 1.007 (0.878 – 1.155 ; 0.919)	0.118)

Supplementary table 2: Relationship between scoring in the PSS, STAI, and/or EPDS with infants in the lower 10th birth centile, neonatal resuscitations and NICU Admissions. Binary logistic regression shows no significant difference between groups $P>0.05$. Adjusted for maternal age, BMI and social class.

Supplementary figure 2: Intercorrelations of questionnaire scores



*Supplementary figure 2: Correlation matrices showing relationship between PSS, STAI and EPDS scores. Pearson correlation shows each questionnaire is significantly correlated. PSS and STAI ($r = 0.521$; $P < 0.001$ ***), PSS and EPDS ($r = 0.724$; $P < 0.001$ ***) and STAI and EPDS ($r = 0.678$; $P < 0.001$ ***). RStudio.*

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<i>Perceived Stress Scale</i>		
	OR (CI ; <i>p</i> -value)	aOR (CI ; <i>p</i> -value)
1 adverse outcome	0.669 (-1.245 – 0.442; 0.351)	0.648 (-1.302 - 0.435; 0.328)
2 adverse outcomes	0.341 (-3.276 – 1.122; 0.337)	0.335 (-3.310 – 1.124; 0.334)
3 adverse outcomes	0.852 (-2.607 – 2.287; 0.898)	0.878 (-2.628 – 2.468; 0.474)
<i>Stat Trait Anxiety Inventory</i>		
	OR (CI ; <i>p</i> -value)	aOR (CI ; <i>p</i> -value)
1 adverse outcome	0.914 (-0.974 – 0.794; 0.842)	0.860 (-1.076 – 0.773; 0.748)
2 adverse outcomes	1.325 (-1.492 – 2.055; 0.756)	1.440 (-1.445 – 2.174; 0.693)
3 adverse outcomes	1.325 (-2.174 – 2.736; 0.822)	0.809 (-2.769 – 2.346; 0.871)
<i>Edinburgh Postnatal Depression Scale</i>		
	OR (CI ; <i>p</i> -value)	aOR (CI ; <i>p</i> -value)
1 adverse outcome	0.914 (-0.974 – 0.794; 0.842)	0.914 (-1.019 – 0.839; 0.849)
2 adverse outcomes	--	--
3 adverse outcomes	1.325 (-2.174 – 2.736; 0.822)	1.090 (-2.517 – 2.690; 0.948)
<i>Cumulative</i>		
	OR (CI ; <i>p</i> -value)	aOR (CI ; <i>p</i> -value)
1 adverse outcome	1.025 (-1.056 – 1.105; 0.965)	0.986 (-1.148 – 1.120; 0.981)
2 adverse outcomes	--	--

3 adverse outcomes	2.818 (-1.449 – 3.521; 0.414)	1.610 (-2.143 – 3.094; 0.722)
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Supplementary table 3: Odds ratios assessing the relationship between prenatal distress and number of newborn adversities. Newborns were grouped into number of adverse birth outcomes based on six parameters (a) Admission to the NICU (b) Newborn Resuscitation received (c) Delivered before 37 weeks gestation (d) 5 minute Apgar score ≤ 7 (e) Birth Temperature $< 36.5^{\circ}\text{C}$ and (f) Birth Centile ≤ 10 or ≥ 90 . Ordinal logistic regression analysis revealed no significant effect ($P > 0.05$). Adjusted for maternal age, BMI and social class.

Supplementary table 4: Linear regression analysis of placental HSD11B2 mRNA expression with maternal distress, demographics and neonatal outcomes

HSD11B2	R²	β- coefficient	95% CI	p-value
Birthweight	0.019	0.137	-0.783 – 1.547	0.505
Placental weight	0.037	0.119	-0.144 – 0.382	0.360
PWR	0.030	0.173	0.00 – 0.00	0.408
Birthweight centiles	0.012	0.109	-0.068 – 0.116	0.597
1 min Apgar	0.012	0.109	-0.002 – 0.003	0.597
5 min Apgar	0.011	0.103	-0.001 – 0.002	0.617
Birth Temperature	0.003	0.054	-0.001 – 0.001	0.794
Gravidity	0.000	-0.009	-0.009 – 0.009	0.964
Maternal Age	0.004	-0.064	-0.647 – 0.472	0.472
Maternal BMI	0.062	-0.248	-0.001 – 0.212	0.212

	0.000			
Social Class	0.009	-0.095	-0.954	– 0.636
	0.594			
PSS	<i>0.137</i>	<i>-0.370</i>	<i>-0.051</i>	– <i>0.058</i>
	<i>0.001</i>			
STAI	0.070	-0.265	-0.025	– 0.181
	0.005			
EPDS	0.068	-0.260	-0.038	– 0.190
	0.008			

Supplementary table 4: Placental HSD11B2 expression and continuous variables. Linear regression analysis. $P > 0.05$.

Supplementary table 5: Linear regression analysis of placental NR3C1 mRNA expression with maternal distress, demographics and neonatal outcomes

NR3C1	R²	β- coefficient	95% CI	p-value
Birthweight	0.083	-0.288	-1961 – 325.796	0.153
Placental weight	0.159	-0.398	-790.258 - -2.667	0.049
PWR	0.086	-0.293	-0.867 – 0.146	0.155
Birthweight centiles	0.170	-0.412	-180 - -6.380	0.036
1 min Apgar	0.004	-0.064	-2.870 – 2.111	0.756
5 min Apgar	0.00	0.010	-1.714 – 1.794	0.962
Birth Temperature	0.038	-0.195	-1.267 – 0.455	0.340
Gravidity	0.003	-0.054	-9.854 – 7.583	0.791
Maternal Age	0.00	0.015	-547.008 – 588.035	0.941
Maternal BMI	0.023	0.151	-0.292 – 0.635	0.453
Social Class	0.005	0.074	-644.397 – 955.528	0.715
PSS	0.075	0.273	-8.437 – 45.959	0.168
STAI	0.003	0.052	-13.496 – 17.405	0.797
EPDS	0.007	0.084	-18.893 – 28.563	0.678

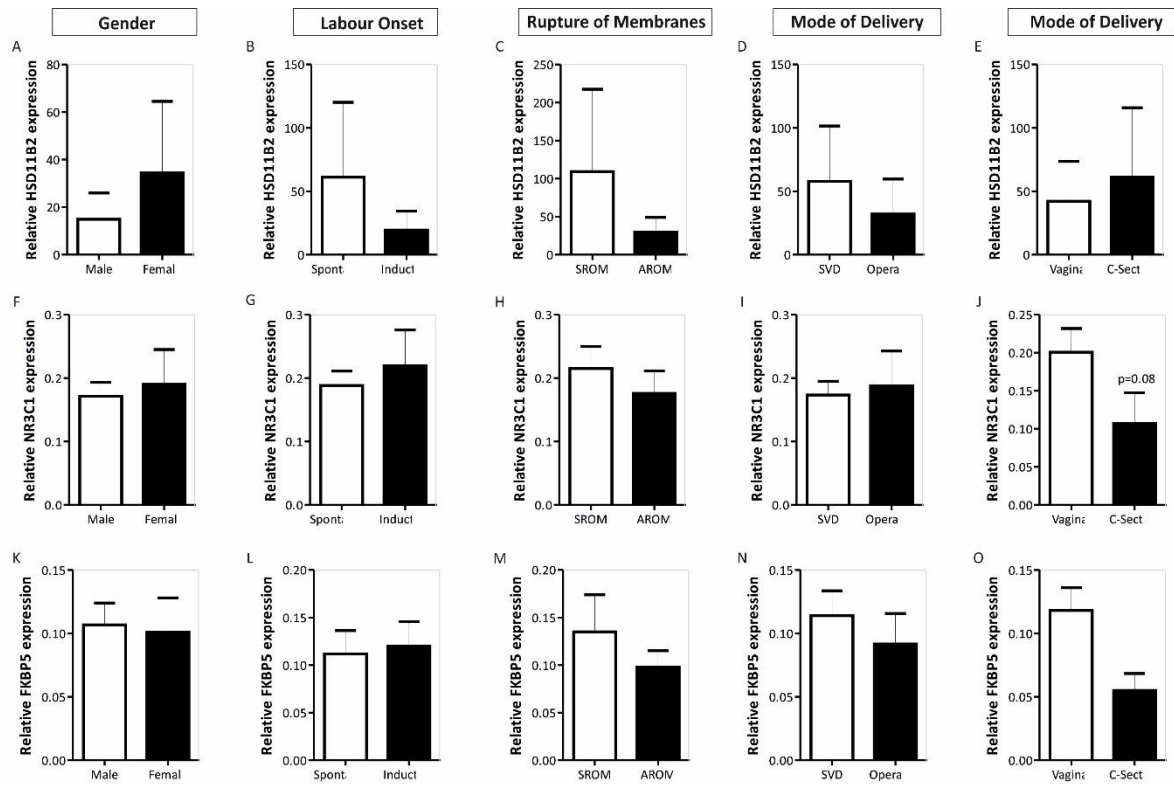
Supplementary table 5: Placental NR3C1 expression and continuous variables. Linear regression analysis. Placental weight and birthweight centiles associated with NR3C1 levels. P < 0.05 *.

Supplementary table 6: Linear regression analysis of placental FKBP51 mRNA expression with maternal distress, demographics and neonatal outcomes

FKBP51	R²	β- coefficient	95% CI	p-value
Birthweight	0.033	-0.183	-2955.102 – 1147.112	0.372
Placental weight	0.109	-0.330	-1010.482 – 106.235	0.107
PWR	0.020	-0.140	-0.959 – 0.487	0.506
<i>Birthweight centiles</i>	<i>0.150</i>	<i>-0.387</i>	<i>-308.452 – 0.616</i>	<i>0.051</i>
1 min Apgar	0.011	0.107	-3.244 – 5.473	0.603
5 min Apgar	0.002	0.05	-2.714 – 3.444	0.809
Birth Temperature	0.015	-0.122	-1.985 – 1.086	0.551
<i>Gravidity</i>	<i>0.012</i>	<i>-0.122</i>	<i>-19.559 – 11.174</i>	<i>0.579</i>
<i>Maternal Age</i>	<i>0.137</i>	<i>-0.370</i>	<i>-47.048 – 1.302</i>	<i>0.063</i>
Maternal BMI	0.185	0.430	3.069 – 42.498	0.025
Social Class	0.023	0.153	-862.086 – 1893.458	0.448
PSS	0.038	0.194	-25.554 – 72.702	0.332
STAI	0.008	0.088	-21.420 – 33.170	0.661
EPDS	0.045	0.212	-1.231 – 3.962	0.289

Supplementary table 6: Placental FKBP5 expression and continuous variables. Linear regression analysis. Maternal BMI positively associated with FKBP5 levels. P < 0.05 *.

Supplementary figure 3: Placental gene expression, gender and obstetric outcomes



Supplementary figure 3: Expression of placental HSD11B2, NR3C1 and FKBP5 in relation newborn sex and obstetric outcomes. No significant differences between groups. Unpaired Student's t-test. $P < 0.005$. Spontaneous (Spont), Induction (Induct), Spontaneous rupture of membranes (SROM), Artificial Rupture of membranes (AROM), Spontaneous vaginal delivery (SVD), Operative delivery (Opera) Vaginal delivery (Vagin) and C-Section delivery (C-Sect).