SUPPLEMENTARY MATERIAL

Supplementary Figure 1: Leucine reduces brain kynurenine. ***A,B*** Mean tryptophan and kynurenine in brains (± SEM) of mice treated with 50 mg/kg leucine or vehicle immediately before and 6 h after LPS or phosphate-buffered saline (PBS) (n = 5-7). ***C,D*** Mean tryptophan and kynurenine in plasma (± SEM) of mice treated with 50 mg/kg leucine or vehicle immediately before and 6 h after LPS or phosphate-buffered saline (PBS) (n = 5-7). $^{*}p \leq 0.05$, $^{**}p \leq 0.01$ for LPS vs PBS main effects. $^{\#\#}p \leq 0.01$, $^{\#\#\#}p \leq 0.0001$ for leucine vs vehicle main effects.

Supplementary Figure 2: LPS induces sickness. ***A,B*** Mean hourly body weight change (g/h) and food consumption (g/h) (± SEM) of mice treated with leucine or vehicle immediately before and 6 h after LPS or phosphate-buffered saline (PBS) (n ≥ 15 per group). ***C,D*** Mean quadrant entries and rears (± SEM) of mice treated with leucine or vehicle immediately before and 6 h after LPS or PBS (n ≥ 14 per group). $^{*}p \leq 0.05$, for LPS vs PBS main effects. $^{\#\#\#}p \leq 0.0001$ for leucine vs vehicle main effects. $^{+}p \leq 0.05$ for leucine simple comparisons.

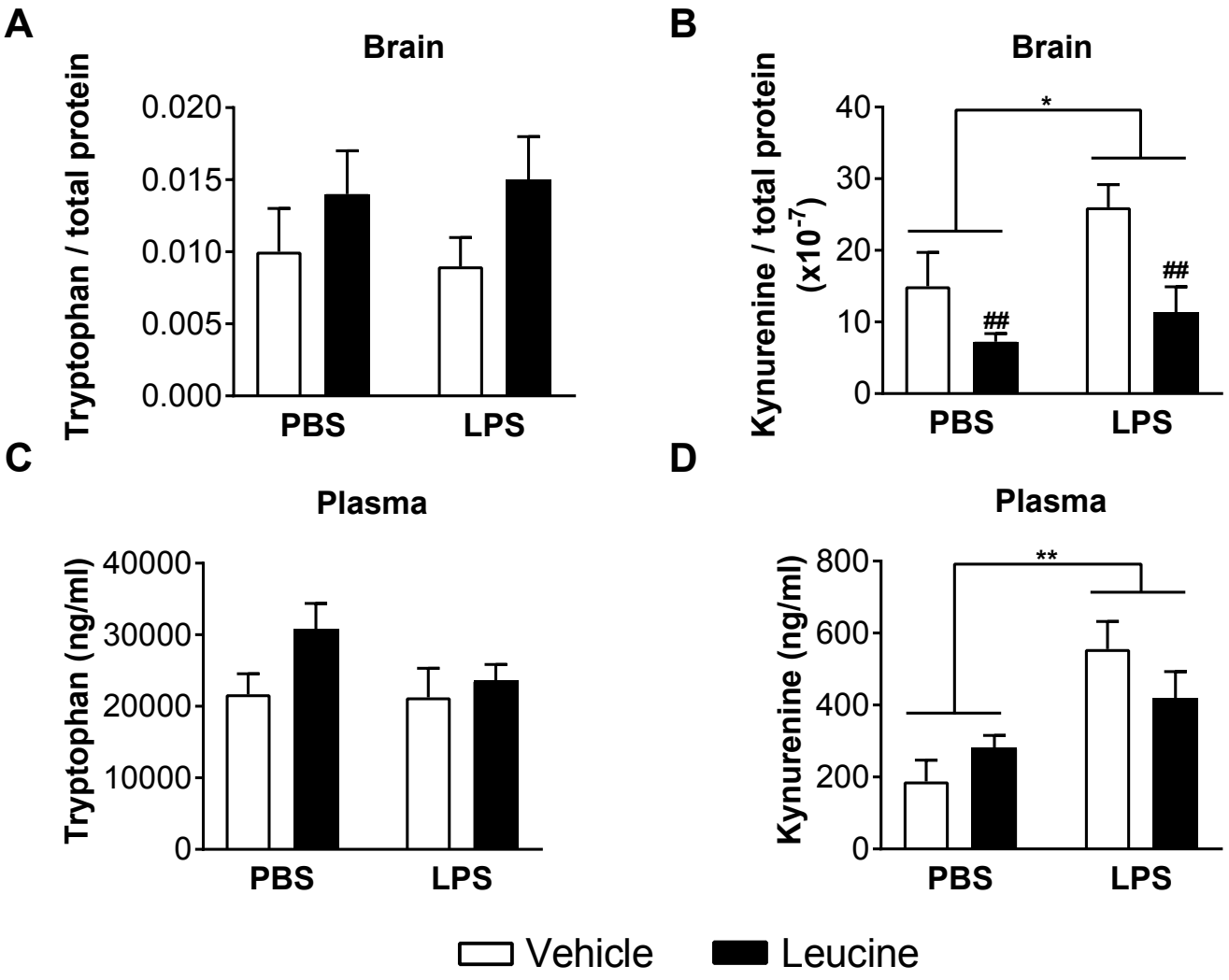
Supplementary Figure 3: LPS increases hepatic inflammation and IDO activation. Mean IL-1β, IL-6, TNFα, IL-10, and IDO mRNA levels (fold change of control at each time point) (± SEM) in livers of mice treated with leucine or vehicle and LPS or phosphate-buffered saline (PBS) at 6 and 27 h after LPS (n ≥ 5 per group). $^{*}p \leq 0.05$, $^{**}p \leq 0.01$, $^{***}p \leq 0.0001$ for LPS vs PBS comparisons. $^{\#}p \leq 0.05$ for leucine main effects.

Supplementary Figure 4: LPS increases central inflammation and IDO activation. Mean IL-1β, IL-6, TNFα, and IDO mRNA levels (fold change of control at each time point) (± SEM) in prefrontal cortices of mice treated with leucine or vehicle and LPS or phosphate-buffered saline (PBS) at 6 and 27 h after LPS (n ≥ 5 per group). *$p \leq 0.05$, **$p \leq 0.01$, ***$p \leq 0.0001$ for LPS vs PBS comparisons. $^{\#}p \leq 0.05$ for leucine main effects.

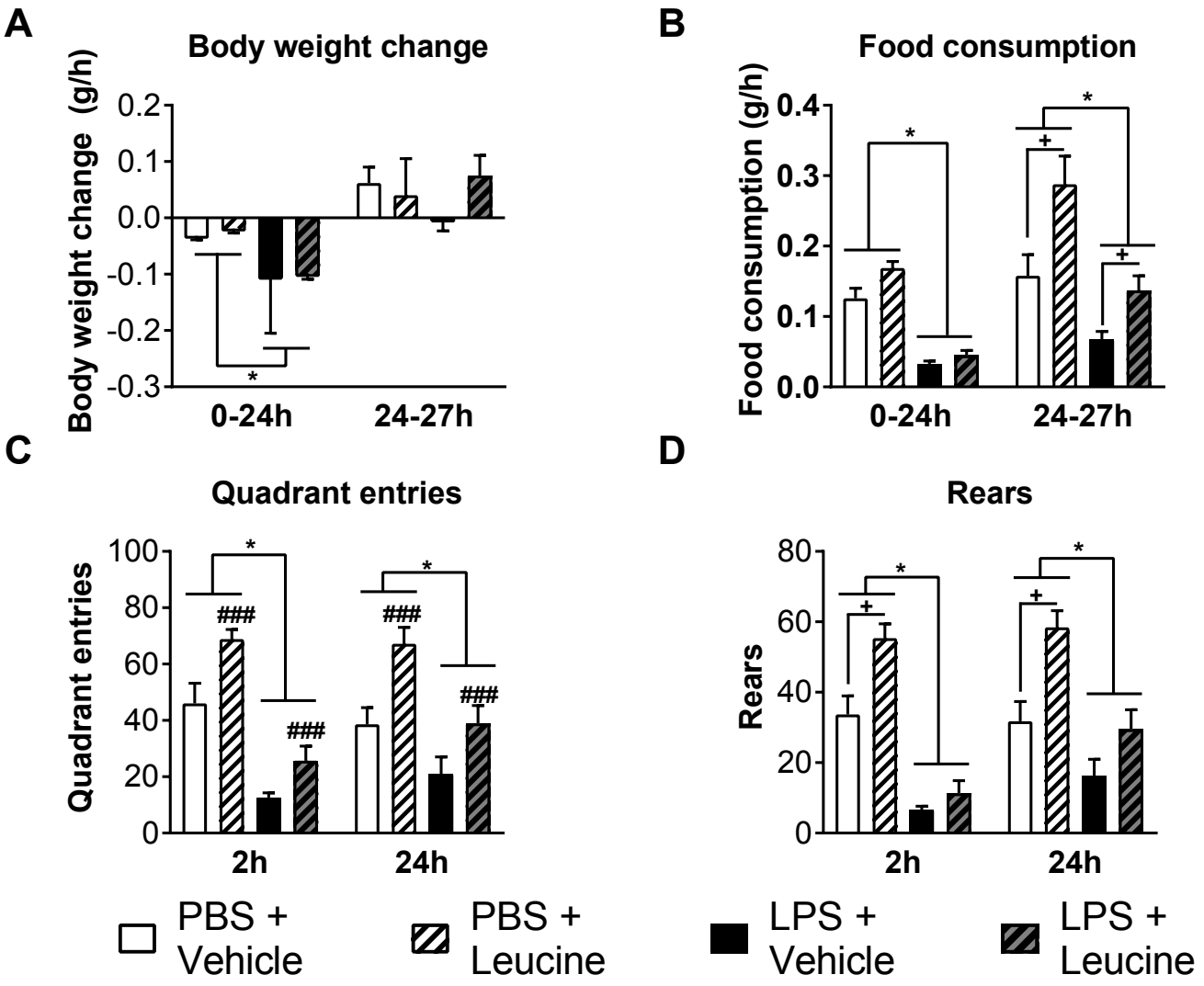
Supplementary Figure 5: LPS increases hippocampal inflammation and induces IDO activation without interference by leucine. Mean IL-1β, IL-6, Tnfα, and IL-10 mRNA levels (fold change of control) (± SEM) in the hippocampi of mice treated with leucine or vehicle immediately before and 6 h after LPS or phosphate-buffered saline (PBS) 27 h after LPS (n ≥ 7 per group). **$p \leq 0.01$, ***$p \leq 0.0001$ for LPS vs PBS comparisons.

Supplementary Table 1: ANOVA statistics for all cytokine and IDO mRNA data in the liver, prefrontal cortex (PFC) and hippocampus at 6 and 27 h after LPS. n.s. = not significant; n.d. = not detectable; n.m. = not measured.

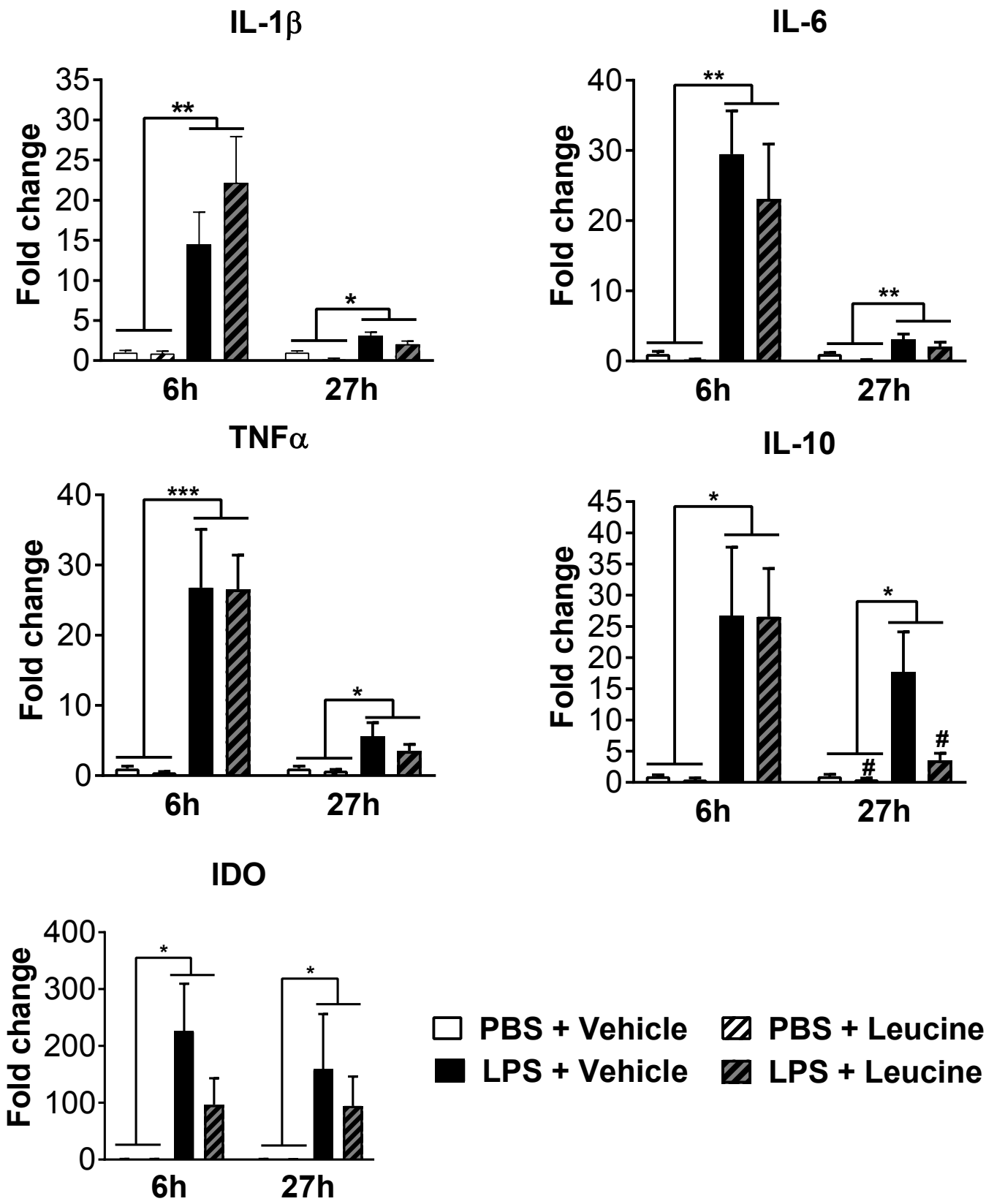
Supplementary Figure 6: LPS increases LAT1 mRNA. Mean SCL3A2 and SLC7A5 mRNA levels (fold change of control) (± SEM) in prefrontal cortices of mice treated with leucine or vehicle and LPS or phosphate-buffered saline (PBS) at 6 h after LPS (n = 4-5 per group).



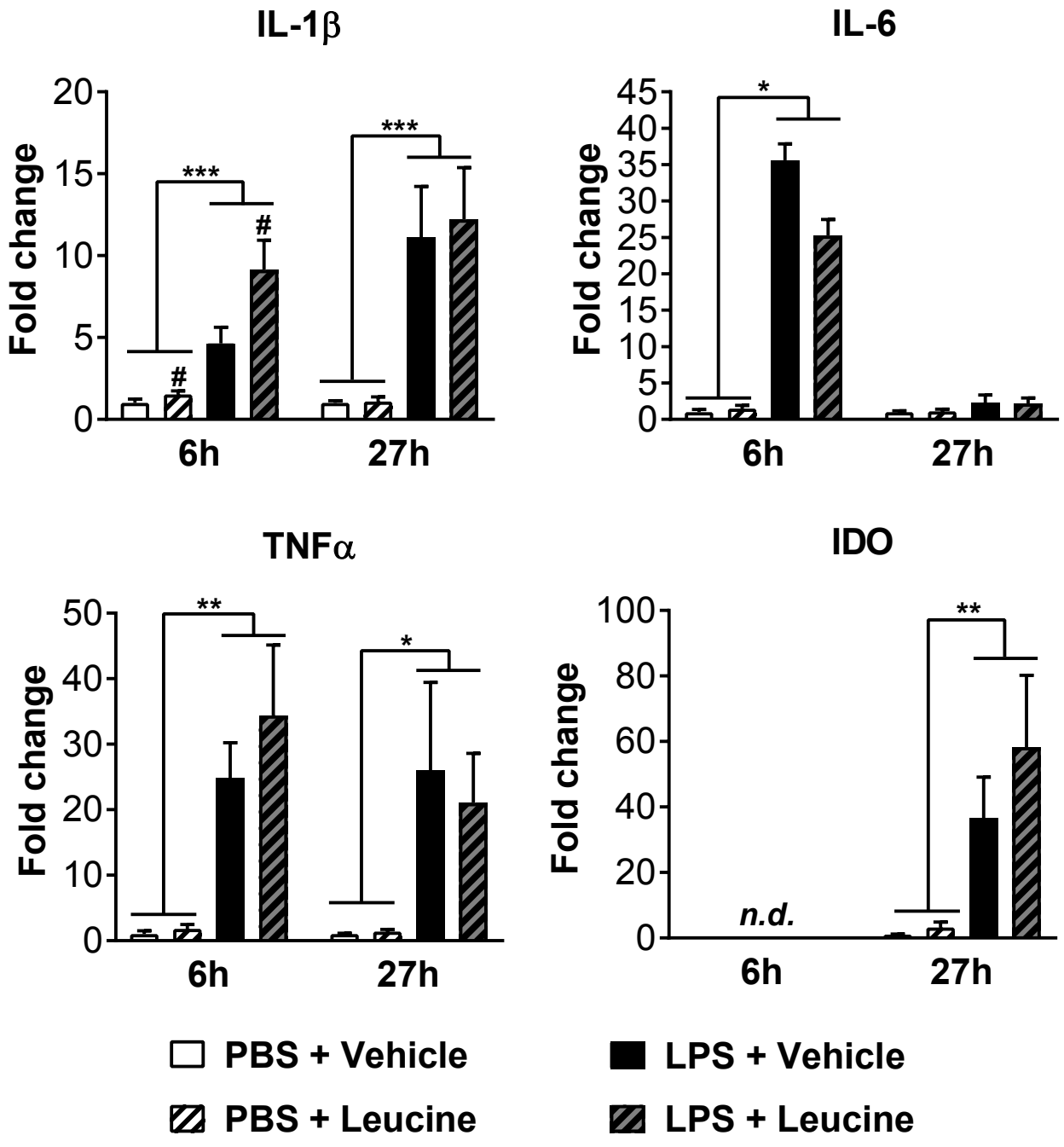
Supplementary Figure 1.



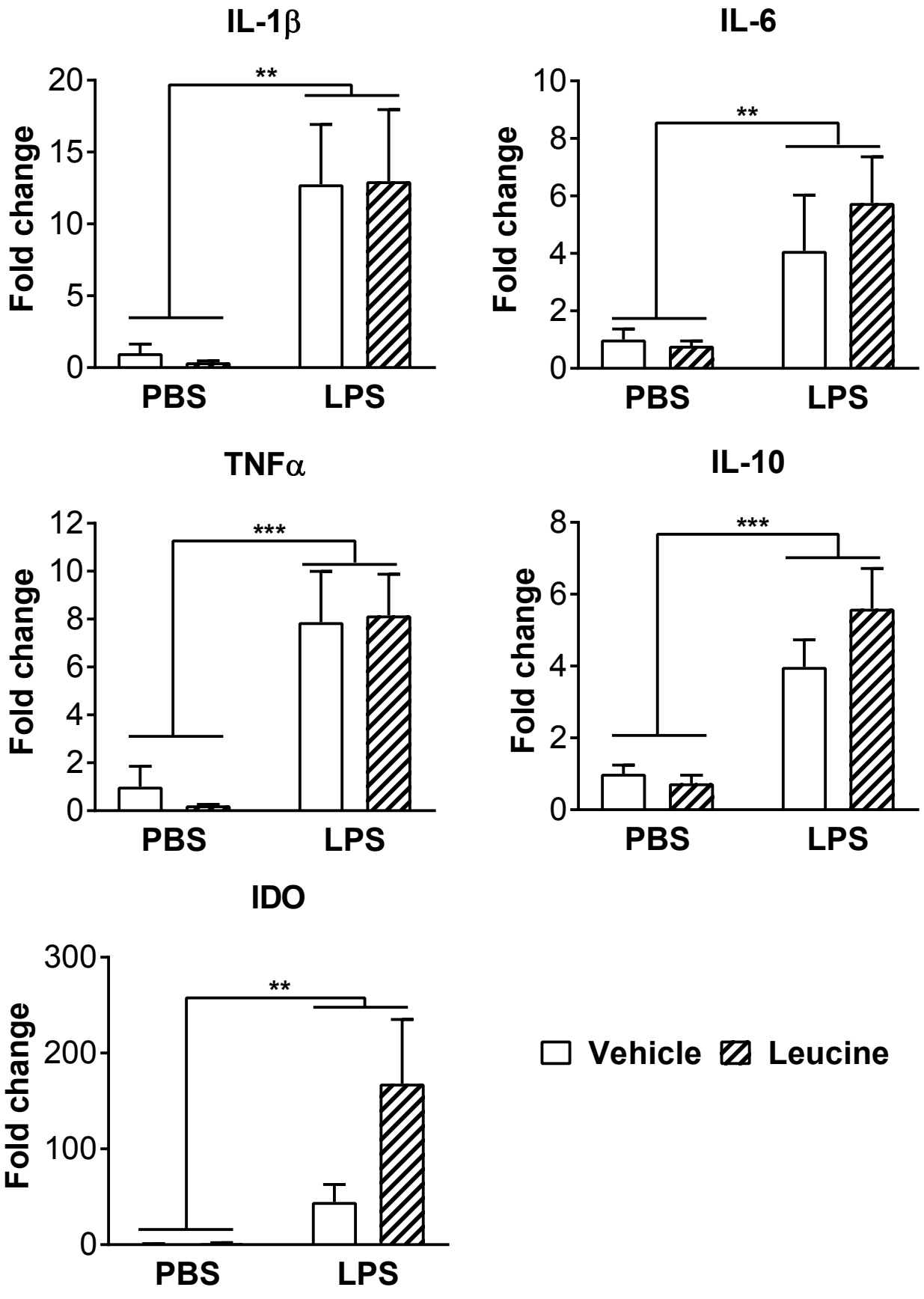
Supplementary Figure 2.



Supplementary Figure 3.



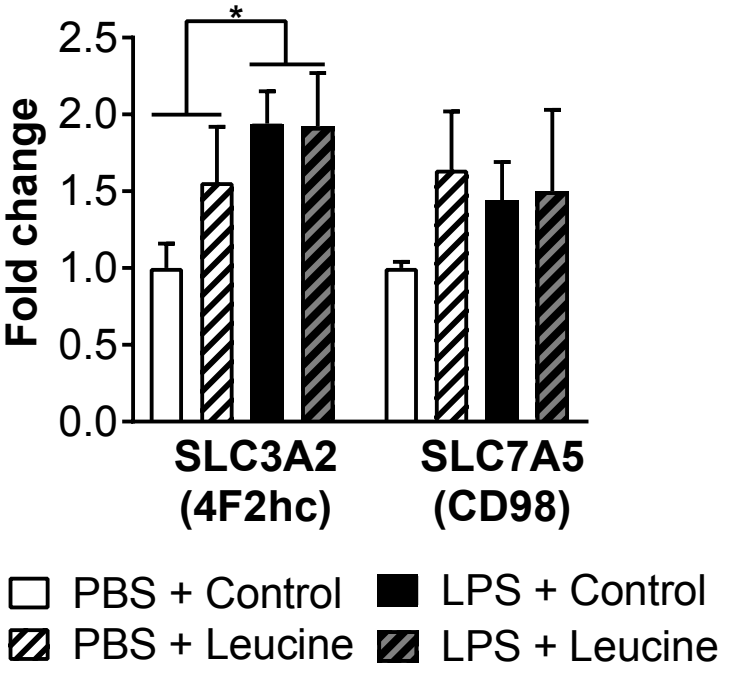
Supplementary Figure 4.



Supplementary Figure 5.

Supplementary Table 1: Statistical information relating to cytokines assessed in the liver, prefrontal cortex and hippocampus.

	Main Effect of LPS		Main Effect of Leucine		LPS x Leucine Interaction	
	6 h	**27 h**	**6 h**	**27 h**	**6 h**	**27 h**
Liver IL-6	$F_{(1,21)} = 18.4$, $p < 0.01$	$F_{(1,48)} = 16.19$, $p < 0.01$	n.s	n.s	n.s	n.s
Liver IL-1β	$F_{(1,23)} = 18.5$, $p < 0.001$	$F_{(1,49)} = 6.13$, $p < 0.05$	n.s	n.s	n.s	n.s
Liver TNFα	$F_{(1,23)} = 24.2$, $p < 0.0001$	$F_{(1,48)} = 10.72$, $p < 0.01$	n.s	n.s	n.s	n.s
Liver IL-10	See interaction column	$F_{(1,27)} = 8.53$, $p < 0.01$	n.s	$F_{(1,27)} = 8.53$, $p < 0.01$	$F_{(1,20)} = 7.53$, $p < 0.001$	$F_{(1,27)} = 8.53$, $p < 0.01$
Liver IDO	$F_{(1,20)} = 8.93$, $p < 0.01$	$F_{(1,50)} = 4.657$, $p < 0.05$	n.s	n.s	n.s	n.s
PFC IL-6	$F_{(1,14)} = 9.69$, $p < 0.01$	n.s.	n.s	n.s	n.s	n.s
PFC IL-1β	$F_{(1,15)} = 25.59$, $p = 0.01$	$F_{(1,31)} = 18.91$, $p < 0.0001$	n.s	n.s	n.s	n.s
PFC TNFα	$F_{(1,15)} = 19.25$, $p < 0.01$	$F_{(1,31)} = 6.48$, $p < 0.05$	n.s	n.s	n.s	n.s
PFC IL-10	n.s.	$F_{(1,32)} = 6.88$, $p < 0.05$	n.s	n.s	n.s	n.s
PFC IDO	n.d.	$F_{(1,30)} = 11.31$, $p < 0.01$	n.s	n.s	n.s	n.s
Hippocampus IL-6	n.m	$F_{(1,31)} = 8.45$, $p < 0.01$	n.s	n.s	n.s	n.s
Hippocampus IL-1β	n.m.	$F_{(1,29)} = 10.81$, $p < 0.01$	n.s	n.s	n.s	n.s
Hippocampus TNFα	n.m.	$F_{(1,31)} = 23.32$, $p < 0.0001$	n.s	n.s	n.s	n.s
Hippocampus IL-10	n.m.	$F_{(1,28)} = 26.91$, $p < 0.0001$	n.s	n.s	n.s	n.s
Hippocampus IDO	n.m.	($F_{(1,31)} = 6.396$, $p < 0.01$	n.s	n.s	n.s	n.s



Supplementary Figure 6.