

Increased systemic microbial translocation is associated with depression during early pregnancy

Zejun Zhou, Constance Guille, Elizabeth Ogunrinde et al.

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- Impact Factor: **3.917**
- 5-Year Impact Factor: **4.475**



Background


Peripartum depression is a disorder that occurs in 8–15% of childbearing women.

The first trimester is the most vulnerable since the most important changes in women's hormonal system and mental condition take place.


Study hypothesis:

Microbial translocation is associated with depression during pregnancy.

Nothing about early pregnancy...



Which factor is primary ??



Depression + alteration of sex hormones => disruption of mucosal barriers => increased microbial translocation+systemic inflammation

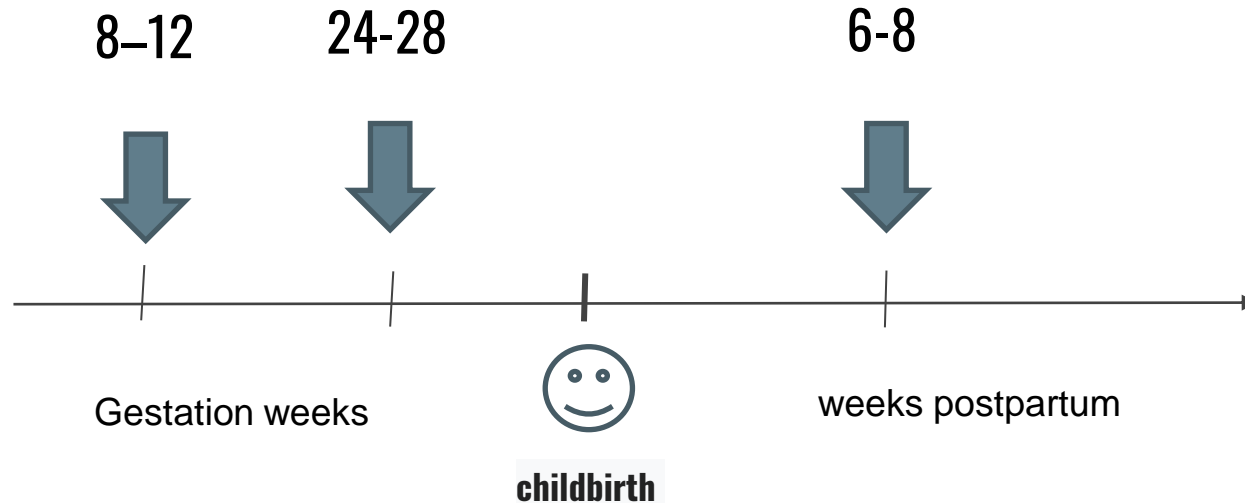
✓ Association does not imply causality !

Increased microbial translocation+systemic inflammation => Depression + alteration of sex hormones

Works as well for: **Microbial translocation is associated with depression during pregnancy ...**


Study design

Longitudinal study, 3 control time-points:



Participants

Total number that was included into analysis = 28



No data about actual sample size...

Inclusion criteria:

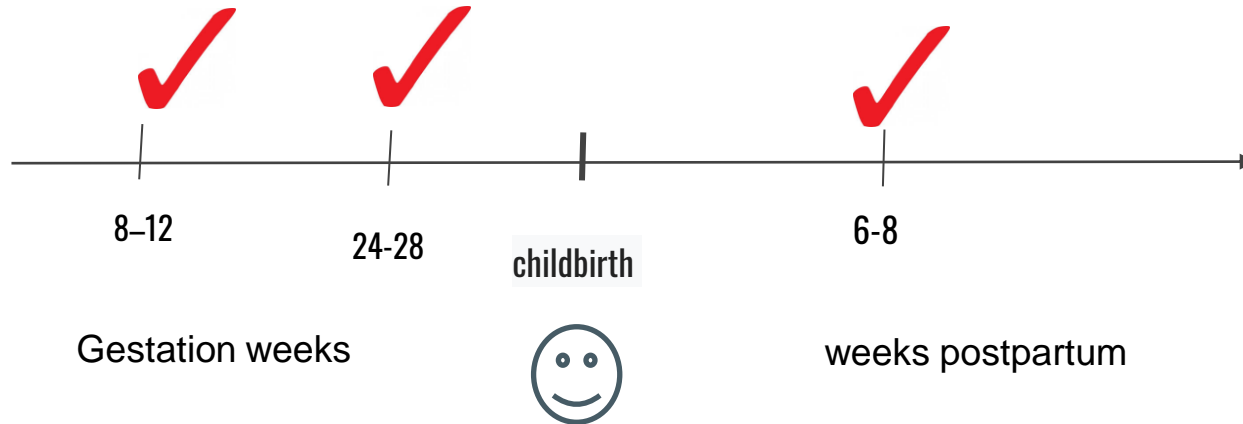
- pregnant women receiving routine obstetrical care
- age > 18
- Gestation < 12 weeks at the first visit

Non-inclusion criteria:

- age < 18
- weeks of gestation > 12 at the first visit
- Not signed informed consent

Methods

- 1. Depression Scale (**EPDS**)
- 1. Biomarkers of microbial translocation in blood: **LPS** (endotoxin)
- 1. Biomarkers of systemic inflammation in blood: $\text{TNF-}\alpha$, IL-6, IL- β , MCP/CCL2



Edinburgh Postnatal Depression Scale (EPDS)

10 items, past 7 days

1. I have been able to laugh and see the funny side of things

As much as I always could (score of 0)
Not quite so much now (score of 1)
Definitely not so much now (score of 2)
Not at all (score of 3)

2. I have looked forward with enjoyment to things

As much as I ever did (score of 0)
Rather less than I used to (score of 1)
Definitely less than I used to (score of 2)
Hardly at all (score of 3)

3. I have blamed myself unnecessarily when things went wrong

Yes, most of the time (score of 3)
Yes, some of the time (score of 2)
Not very often (score of 1)
No, never (score of 0)

4. I have been anxious or worried for no good reason

No, not at all (score of 0)
Hardly ever (score of 1)
Yes, sometimes (score of 2)
Yes, very often (score of 3)

5. I have felt scared or panicky for no very good reason

Yes, quite a lot (score of 3)
Yes, sometimes (score of 2)
No, not much (score of 1)
No, not at all (score of 0)

6. Things have been getting on top of me	Yes, most of the time I haven't been able to cope at all (score of 3) Yes, sometimes I haven't been coping as well as usual (score of 2) No, most of the time I have coped quite well (score of 1) No, I have been coping as well as ever (score of 0)
7. I have been so unhappy that I have had difficulty sleeping	Yes, most of the time (score of 3) Yes, sometimes (score of 2) Not very often (score of 1) No, not at all (score of 0)
8. I have felt sad or miserable	Yes, most of the time (score of 3) Yes, quite often (score of 2) Not very often (score of 1) No, not at all (score of 0)
9. I have been so unhappy that I have been crying	Yes, most of the time (score of 3) Yes, quite often (score of 2) Only occasionally (score of 1) No, never (score of 0)
10. The thought of harming myself has occurred to me	Yes, quite often (score of 3) Sometimes (score of 2) Hardly ever (score of 1) Never (score of 0)

Source: Edinburgh Postnatal* Depression Scale (EPDS Cox et al 1987).

(*Developed as the Edinburgh Postnatal Depression Scale but can be used in both pregnancy and postnatal period to assess for possible depression and anxiety. Questions 3, 4 and 5 relate to possible symptoms of anxiety disorders)

Groups

A. Depressed (n=14)

Participant ID	EPDS scores		
	Visit 1	Visit 2	Visit 3
1	1	13	5
2	9	14	7
3	14	18	8
4	16	13	13
5	11	12	19
6	6	10	10
7	6	12	17
8	14	11	13
9	9	15	11
10	8	14	13
11	7	13	13
12	8	11	13
13	10	6	13
14	22	17	19

B. Healthy (n=14) *Control*

Participant ID	EPDS scores		
	Visit 1	Visit 2	Visit 3
1	9	3	7
2	3	7	5
3	0	0	0
4	9	5	3
5	0	0	0
6	4	0	1
7	5	5	0
8	0	0	0
9	6	5	4
10	6	4	6
11	5	4	7
12	0	1	0
13	2	3	1
14	2	1	1

EPDS >10= Depression

Sample' demographic and clinical characteristics 1.

	Healthy controls	Depressed patients	P value ^a
Numbers of subjects	14	14	
Age (years) median ^b	30 (25–32)	29 (23–33)	0.61
Maternal BMI at visit 1 (kg/m ²) ^b	33.0 (26.3–38.3)	32.5 (25.5–37.3)	0.92
Gravidity ^b	2.0 (2.0–3.3)	2.5 (1.0–4.0)	0.97
Parity ^b	1.0 (0.8–1.0)	0.5 (0.0–1.3)	0.33
Total gestation weeks ^b	39.0 (37.8–40.0)	39.5 (38.0–40.3)	0.39
Baby birth weight (oz) ^b	115.5 (108.8–130.3)	122.5 (107.5–136.3)	0.46
Therapies of depression	No	No	
Previous psychiatric disorders	No	No	
Alcohol drinking (past 12 h)	No	No	
Systemic antibiotic treatment (past 6 months)	No	No	
Fetal sex (%)			> 0.99
Male	35.7	42.9	
Female	64.3	57.1	
Delivery type (%)			0.33
Vaginal	85.7	70.0	
Cesarean	14.3	30.0	

Sample' demographic and clinical characteristics 2.

	Healthy controls	Depressed patients	P value ^a
Ethnicity (%)			> 0.99
Caucasian	50.0	50.0	
Africa American	42.9	42.9	
Asian	7.1	7.1	
Education (%)			0.97
Less than high school +	7.1	21.4	
High school	28.6	42.9	
Some college	35.7	28.6	
College or higher	28.6	7.1	
Family income (%)			> 0.99
Less than \$20,000 +	14.3	28.6	
\$20,000–\$49,999	35.7	35.7	
\$50,000–\$74,999	35.7	35.7	
\$75,000 or more	14.3	0.0	
Smokers (%)			0.80
Never	92.9	71.4	
Former	7.1	21.4	
Current	0.0	7.1	

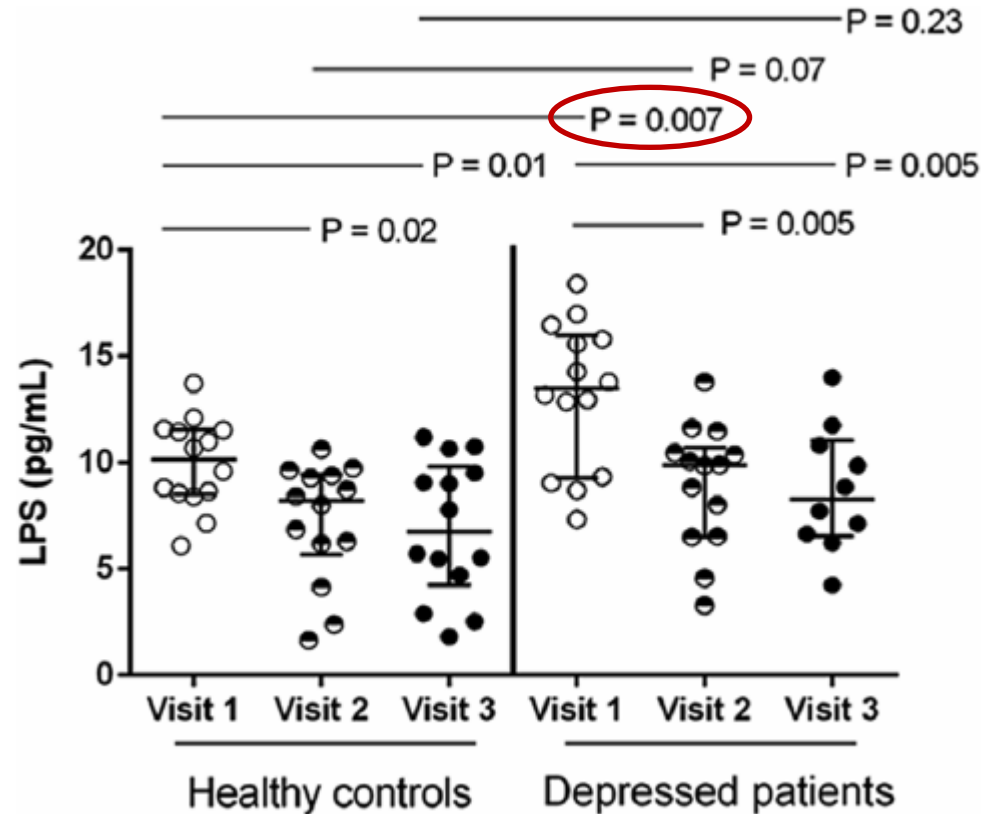
Statistical analysis

Independent variables	Depression 2 categories: yes/ no	
Dependent variables	<i>Primary outcome</i>	<i>Secondary outcomes</i>
	LPS	TNF- α , IL-6, IL-1 β and MCP/CCL2
Confounders	age, race, BMI	

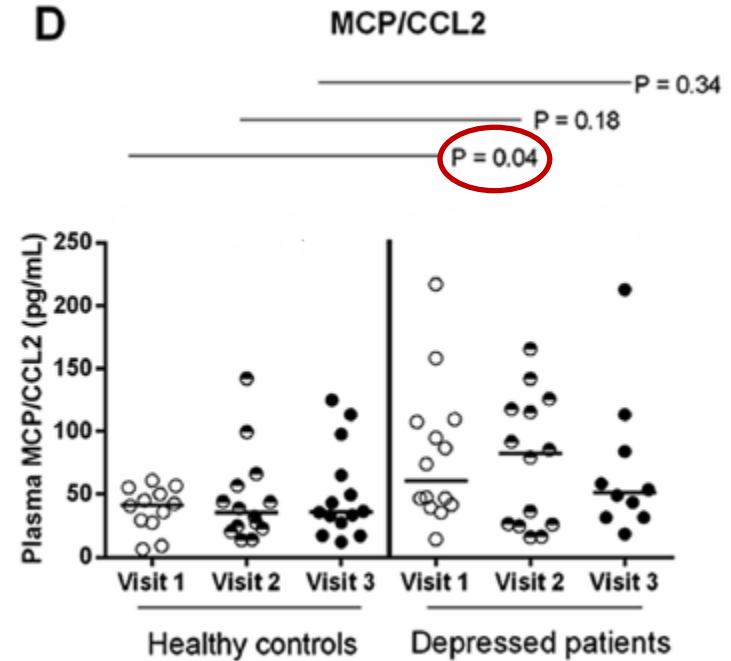
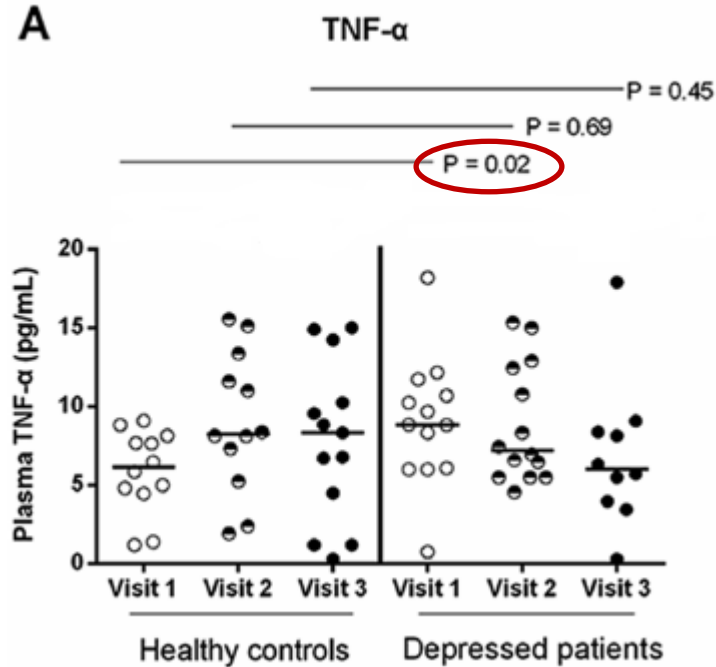
Results

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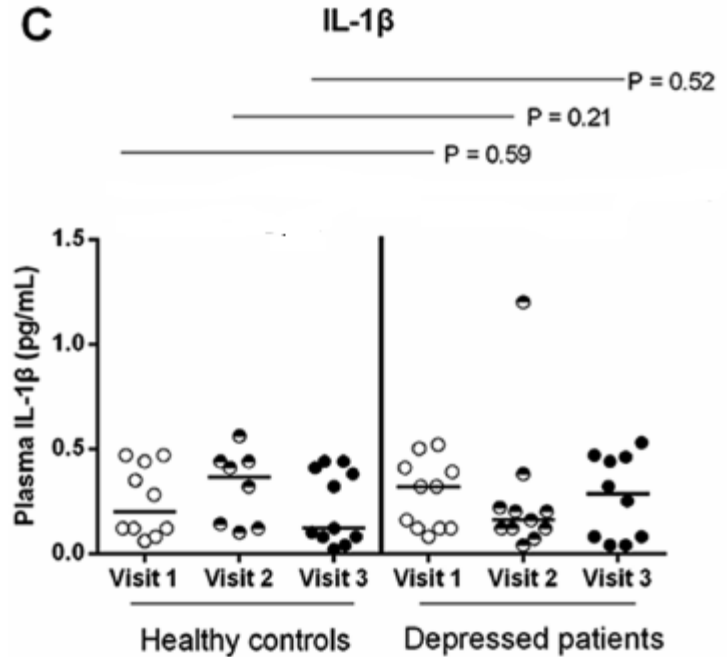
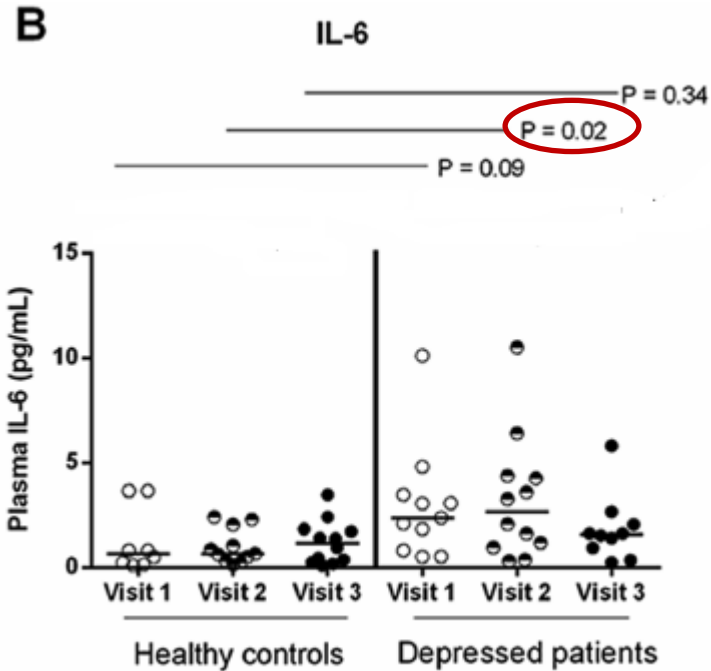
Plasma levels of LPS



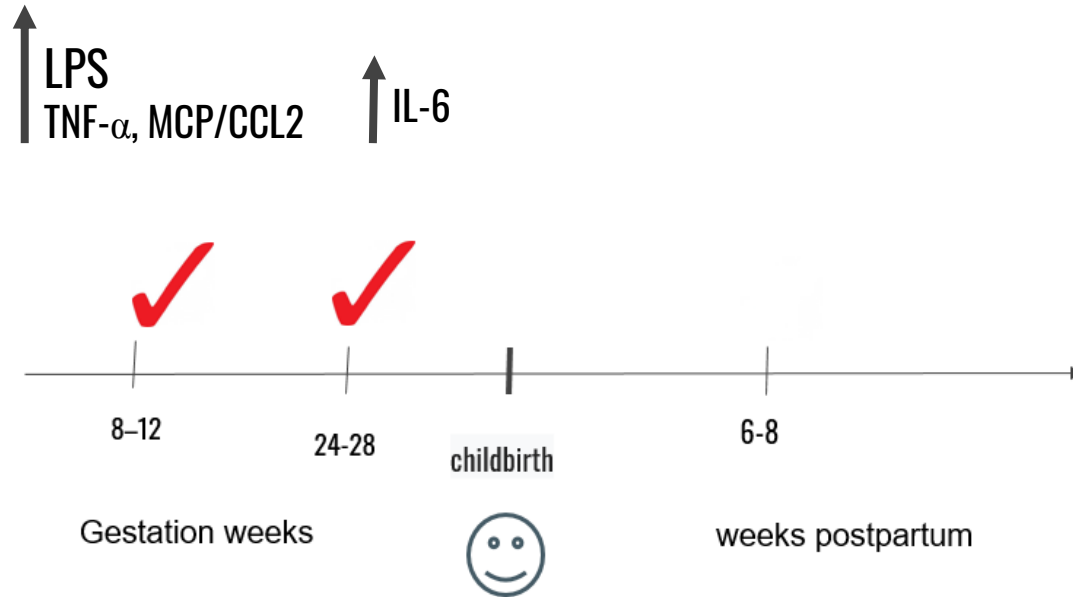
Systemic inflammation markers - TNF- α , MCP



Systemic inflammation markers - IL6, IL-1b



Summary results. Group A vs B



Authors' Conclusion

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Increased systemic microbial translocation is associated with depression during early pregnancy.

Based on our finding, early diagnosis and treatment interventions of depressed mothers may be imperative.

Authors' limitations

- Small sample size
- Several confounding variables (e.g. fetal sex, type II diabetes) may need to be controlled in order to establish a causal inference link between bacterial translocation and postnatal depression.

Discussion. Hypothesis – Design- Results -Conclusion

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1) Was the base hypothesis proved?

Yes, but conclusions are not consistent with the hypothesis and do not follow the results:

Despite the significantly higher level of LPS was found in the group of depressed women at the first control time-point (8-12 gestation weeks), the exact depression was took place predominantly at the second visit (28-30 gestation weeks) and postpartum - not early pregnancy!

Since it only longitudinal study conclusion about treatment strategy can not be done. At least prospective study needed to confirm causality.

No interpretation of data concerning the secondary outcomes (pro-inflammatory cytokines).

Discussion. Materials and methods

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- 1) Were study' groups formed consistent with the aim of the study ?
- 2) Was the sample homogeneous? Any other potential confounding factors?
- 3) Was instrument to assess depression adequate and enough?
- 4) Was methodology to assess microbial translocation and systemic inflammation adequate and enough?
- 5) Why these control time points ? Were they chose correctly??

Resume

1. The article is short and good for discussion
2. After the discussion we identify the most controversial moments of the article, for example, the mismatch in increased level of LPS and presence of depression in pregnant women.
3. The question what appeared first depression or microbial translocation is still opened, and to answer it the research should be supplemented by studying other markers of microbial translocation, sex and stress hormones.

Thanks for your Attention

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Presenter: Ilkovets L.A.
email: ilkovec@list.ru

Mentor: Holodnaya A.N.
email: ancold@inbox.ru