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Repetitive negative thinking during pregnancy and postpartum: Associations with mental health, inflammation, and breastfeeding

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ABSTRACT

Introduction: Repetitive negative thinking (RNT) is a transdiagnostic feature that predicts increased mental health risks, inflammation, and reduced engagement in health promoting behaviors. Depression, anxiety, stress, inflammation, higher body mass index (BMI), and low engagement in health behaviors are associated with adverse outcomes during pregnancy as well as postpartum. However, there is limited literature on the associations between RNT and these contributing factors in the perinatal period, an at-risk time during which women may benefit from clinical interventions directed at RNT.

Methods: This study examined the contribution of RNT to inflammation [interleukin (IL)-6] and breastfeeding duration through mediating indicators of mental health and BMI. Behavioral and biological assessments occurred during late pregnancy as well as at 4–6 weeks, 4 months, 8 months, and 12 months postpartum.

Results: RNT was positively associated with depressive symptoms, anxiety, and perceived stress ($ps \leq .001$) at each assessment timepoint, with the strongest associations observed at the pregnancy assessment and significant, but attenuated, associations during postpartum ($ps < .01$). In modeling of the association between RNT and IL-6, the indirect effect of BMI was significant at each timepoint (95%CIs 0.0013, 0.0052). Women with lower RNT exhibited longer breastfeeding duration ($p = .02$). These effects were not significantly mediated by mental health indicators.

Conclusions: Clinically meaningful relationships, in which RNT predicts mental health, inflammation, and health behavior engagement during pregnancy and postpartum were observed. Clinical interventions to reduce RNT may have unique benefits this time.

Limitations: Further research is warranted to determine if therapies to reduce RNT confer unique benefits for maternal and child health.

1. Introduction

Repetitive negative thinking (RNT) refers to a pattern of thoughts that are intrusive unwanted, unconstructive, negative, and repetitive (Ehring and Watkins, 2008). Prior research has connected RNT to mental health, including both depression and anxiety in non-pregnant adults (Ehring and Watkins, 2008; Zetsche et al., 2018) as well as in women during pregnancy (Hirsch et al., 2020). Furthermore, measures of RNT have been predictive of the severity of depression (Raes, 2012), anxiety (Spinhoven et al., 2018), and perceived stress (Everaert and Joormann, 2020). Depression and anxiety experienced during pregnancy are associated with preterm birth (Staneva et al., 2015), and small for gestational age neonates (Davalos et al., 2012; Uguz et al., 2019). Similar adverse pregnancy outcomes can occur among pregnant women who experience heightened levels of stress (Buffa et al., 2018; Pais and Pai, 2018; Wadhwa et al., 1993). Such adverse outcomes can impact the health and development of children across their lifespan. Depressive symptoms occur in up to 20 % of pregnant women (Biaggi et al., 2016), and up to 24.6 % of pregnant women experience symptoms of anxiety during the third trimester (Dennis et al., 2017). Furthermore, depression

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and anxiety can affect important health behaviors during pregnancy and postpartum; for example, women with greater depressive symptoms are less likely to start breastfeeding or continue breastfeeding as long compared to similar non-depressed peers (Dias and Figueiredo, 2015; Grigoriadis et al., 2013; Ritchie-Ewing et al., 2019).

Adults with anxiety and depressive disorders exhibit increased inflammation including IL-6, C-reactive protein and fibrinogen (Zainal and Newman, 2021). The transdiagnostic influence of RNT may partially underlay a disruption of inflammation by mental health indicators associated with RNT. Additionally, RNT may influence inflammation through disrupting healthy promoting behaviors (Kornacka et al., 2020; Sala et al., 2019) contributing to an association between RNT and BMI. Indeed, the research on associations between mental health indicators and IL-6 routinely account for BMI as BMI impacts the production of IL-6 in women (Werida et al., 2021), including during pregnancy (Christian and Porter, 2014).

Specific to different mental health indicators, while BMI is often the stronger predictor of IL-6 in models that include depressive symptoms (Ambrósio et al., 2018; Li et al., 2017) the positive association between depressive symptoms and IL-6 persists during pregnancy, even after considering BMI (Christian et al., 2009; Simpson et al., 2016). Additionally, a meta-analysis of studies examining the relationship between anxiety and IL-6 reported an overall positive association with IL-6. For these models, BMI was explored as a continuous variable moderating the association between anxiety and IL-6, but did not significantly contribute to them (Renna et al., 2018). Furthermore, during the third trimester of pregnancy (gestational age M = 35 weeks gestation, SD = 0.8) IL-6 was higher among women with more depressive symptoms or anxiety, however pre-pregnancy BMI (dichotomous split at ≥25), as a covariate predicting IL-6, was not significant in cluster analyses (Osborne et al., 2019). Together these patterns of association suggest there may be associations between mental indicators, BMI, and IL-6 which have different strengths depending on pregnancy status and/or timing of measurement during pregnancy. Furthermore, RNT may be a driving part of these associations, partially through its influence on BMI which mediates the association between RNT and inflammation, a connection also supported by our prior research during pregnancy (Mitchell and Christian, 2019).

Research among pregnant and postpartum women has demonstrated that repetitive negative thinking (measured using the Ruminative Responses Scale) can contribute to antenatal depressive symptoms in women at risk for depression with low social functioning (O'Mahen et al., 2010). Furthermore, a lab induced rumination task impairs parental problem solving and confidence in their ability to problem solve in women with dysphoria (O'Mahen et al., 2015). Similarly, in women with generalized anxiety disorder or major depressive disorder, rumination affects maternal bonding by reducing maternal responsiveness to infant vocalization (Stein et al., 2012). In a study by Müller et al. (2013a), women with unproductive repetitive thinking (a form of RNT measured via a subscale of the Perseverative Thinking Questionnaire) reported greater childcare related anxiety, did not feel as close to their child nor were they as content with having a child. These studies suggest that there are differences in maternal-infant bonding in women associated with RNT related symptoms, exacerbated in those with mental health symptoms, to the degree to which those with higher RNT may be less responsive to their infant's behavior. However, these studies did not assess the connection between RNT and breastfeeding behavior. Breastfeeding has been associated with better maternal-child bonding (Roth et al., 2021), which may be related to differences in activation of brain regions in mothers (Kim et al., 2011). Furthermore there is some evidence that anxiety reduces breastfeeding duration (Hoff et al., 2019). Additionally, a meta-analysis by Clancy et al. (2016) connected perseverative cognition, an overarching term which includes RNT, to an increased likelihood of engaging in risky health behaviors versus health promoting behaviors. As breastfeeding is a health promoting bonding behavior and RNT interferes with bonding, and RNT is likely associated with breastfeeding in a way similar to anxiety, suggesting a negative association with breastfeeding duration. Examining the role of RNT during pregnancy and postpartum may provide insights for preventative intervention that would improve mental health and physical health outcomes, as well as promote health-related behaviors including breastfeeding.

The current study examined associations of RNT with mental health (depressive symptoms, anxiety, and perceived stress), BMI, inflammation (serum interleukin-6; Fig. 1), and breastfeeding duration (Fig. 2) in perinatal women. In this longitudinal study design, assessments were conducted during the 3rd trimester (29–34 weeks gestation) as well as at 4–6 weeks, 4 months, 8 months, and 12 months postpartum. Higher RNT was anticipated to predict elevations in depressive symptoms, anxiety, perceived stress and IL-6 across the assessment period, with stronger associations during pregnancy than postpartum. Furthermore, it was anticipated that the association between RNT and IL-6 would be partially mediated by maternal BMI, depressive symptoms, anxiety, and perceived stress, with the clearest effects in these mediation models observable in postpartum given that maternal weight during pregnancy includes weight of the fetus, placenta, and blood volume changes. Finally, it was anticipated that women who report greater RNT would demonstrate shorter breastfeeding duration. Additionally, the negative association between RNT and breastfeeding would be partially explained by mental health indicators of depressive symptoms, anxiety, and perceived stress.

2. Method

2.1. Study sample

The current investigation is part of a longitudinal observational study approved by The Ohio State University Biomedical Institutional Review Board. Women (N = 83) were recruited from The Ohio State University Wexner Medical Center Prenatal Clinic and the surrounding community of central Ohio from 2016 to 2019. Inclusion criteria included current singleton pregnancy. Exclusion criteria included diagnosis of a fetal anomaly, a major immunological condition, or use of medications with implications for immune function. Women who reported working a night shift were also ineligible due to effects on circadian regulation. Written informed consent was obtained at enrollment and participants received modest compensation for each visit. Visits occurred at the following intervals: 29–34 weeks gestational age (Visit 1), 4–6 weeks postpartum (Visit 2), 4 months postpartum (Visit 3), 8 months postpartum (Visit 4), and 12 months postpartum (Visit 5).

2.2. Measures

2.2.1. Demographic variables

During Visit 1, demographic characteristics including maternal race, age, relationship status, physical health conditions, smoking status, medication use, and annual household income were assessed by self-report. Annual household income was assessed on a 6-point scale from 1 (Less than $15,000) to 6 ($100,000 and above). Education was assessed on a 9-point scale from 1 (Less than 7th grade) to 9 (Some graduate school or higher).

2.2.2. Perseverative Thinking Questionnaire (PTQ)

At Visit 1, the 15-item PTQ was administered to assess repetitive negative thinking. Participants were asked to assess their own experience when they typically think about negative experiences or problems related to statements such as, 'Thoughts come to my mind without me wanting them to,' using a 5-point Likert scale ranging from 0 'never' to 4 'almost always.' The sum of total responses were used in the current study. Prior research using the PTQ has demonstrated high reliability in adults (Ehring et al., 2011). Higher scores on the PTQ indicates greater frequency and impact of RNT.

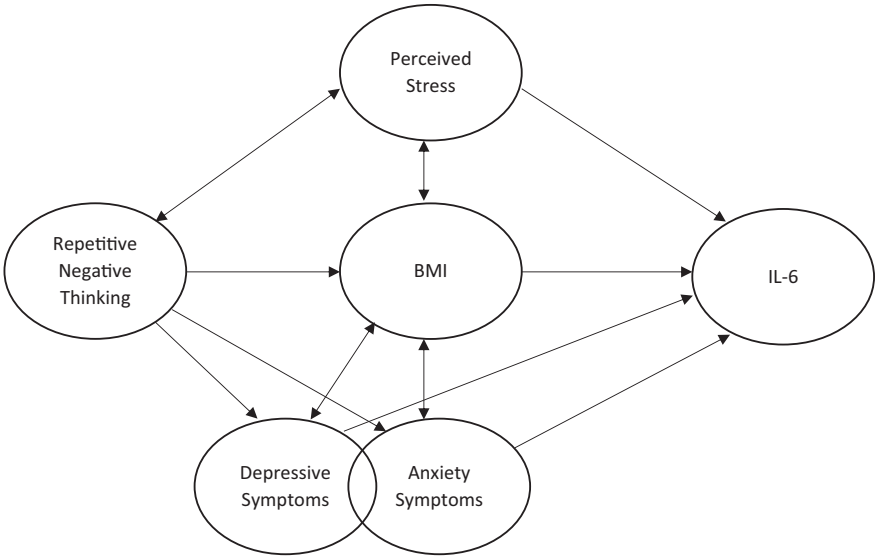

Fig. 1. Model of mediation pathways between repetitive negative thinking and inflammation.

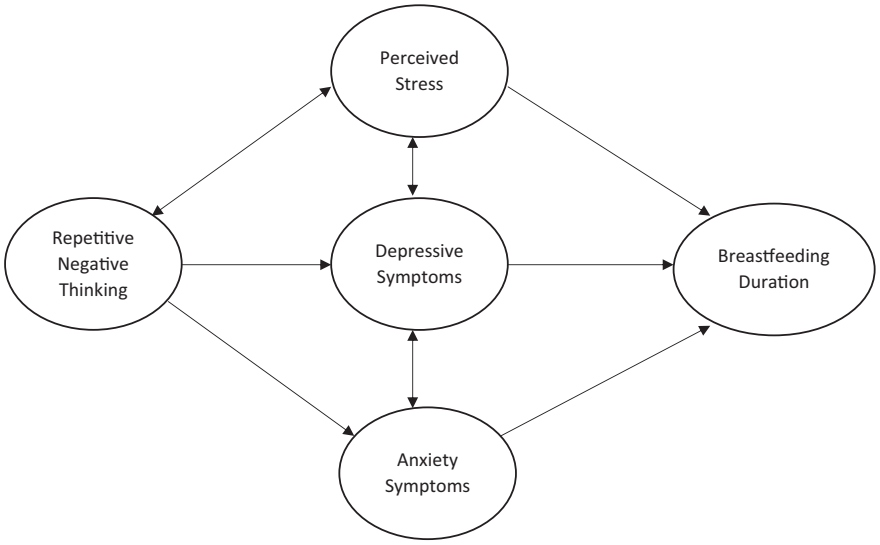

Fig. 2. Model of mediation pathways between repetitive negative thinking and breastfeeding duration.

2.2.3. Quick Inventory of Depressive Symptomatology (QIDS)

At Visits 1–5, the 16-item QIDS was used to assess symptoms of depression over the past week. Participants rated themselves on each feature using a Likert-type scale 0 to 3 among choices particular to the prompting item. For example, for 'Feeling sad,' selections ranged from '0 I do not feel sad' to '3 I feel sad nearly all of the time.' The QIDS has demonstrated strong psychometric properties in studies with adults, with higher scores indicating greater depressive symptoms and clinical relevance for scores of 16 or greater (Rush et al., 2003).

2.2.4. Clinically Useful Anxiety Outcome Scale (CUXOS)

The 20-item CUXOS assessed anxiety-related psychic and somatic symptoms that occurred over the past week during Visits 1–5. Participants rated themselves on prompted items such as, 'I felt scared,' using a Likert type scale from '0 not at all true' to '4 almost always true'. In studies with adults, higher CUXOS scores have shown greater anxiety symptoms with moderate anxiety indicated by scores ≥31 and severe anxiety indicated by scores ≥41 (D'Avanzato et al., 2013; Zimmerman et al., 2010).

2.2.5. Perceived Stress Scale (PSS)

This 10-item measure assessed how often the participant felt stressed or lacking in control during the past month during Visits 1–5. Participants provided ratings from 1 (never) to 5 (very often) (S. Cohen et al., 1983). This scale has shown strong reliability in measuring perceived stress in pregnant women (Hilmert et al., 2008; Wadhwa et al., 1993). Higher summed scores indicate a greater amount of maternal perceived stress.

2.2.6. Interleukin 6 (IL-6)

Blood samples were taken during Visits 1–5, between the hours of 8 and 10 am to control for diurnal variation. Serum IL-6 blood samples were assayed in duplicate for IL-6 (pg/ml) using VPlex kits from Meso Scale Discovery (MSD; 1601 Research Blvd., Rockville, MD). Plates were read by a Meso QuickPlex SQ120 measuring electrochemiluminescence. The lower limit of detection for IL-6 is 0.06 pg/ml, and the intra-assay CV is 4.0 % and the inter-assay CV is 6.4 %. Raw IL-6 values were natural log transformed, then outliers (at ±3 SD from mean of logged values) were removed so that extreme values did not influence results.

2.2.7. Body mass index (BMI)

Body mass index (BMI) is highly associated with IL-6 levels (e.g., Piva et al., 2013). BMI was calculated (kg/m^2) for each participant using height measured at Visit 1, and self-reported pre-pregnancy weight as well as weight measured at Visits 1–5. These measures were used to explore BMI as a mediator of the association between RNT and IL-6.

2.2.8. Breastfeeding duration

Breastfeeding duration in weeks was determined via participant self-report at Visits 2–4. Questions consisted of 'Are you currently breastfeeding?' and 'How old was your baby when you stopped breastfeeding?' The maximum time of breastfeeding reported as currently breastfeeding at the time of their visit, or latest reported for when they had stopped breastfeeding was used (M = 34.18, SD = 18.50, Range = 1 to 52 weeks). Those who were still breasting during Visit 5 were considered to have breastfed for 52 weeks.

2.3. Analytic method

To evaluate the association between the RNT during pregnancy and postpartum periods vs depression, anxiety, stress, inflammation, and breastfeeding behavior, Pearson correlations among PTQ, QIDS, CUXOS, PSS, IL-6 (natural log transformed) at different visits, and breastfeeding duration were calculated. A series of linear mixed models were then used to examine the influence of PTQ, Visit, and the interaction of PTQ and Visit, for QIDS, CUXOS and PSS while consider the association of the repeated measures from the same person at different visit. Different covariance structures for the linear mixed model were examined by comparing fitness indices in Table 4, and unstructured covariance matrix structure was selected for all models (Müller et al., 2013b). The linear mixed model can handle these missing data, which varied between 4.8 % at Visit 1 to 18.1 % at Visit 5, assuming missing at random (MAR) and provide robust estimation. All repeated measures had data available at ≥3 out of 5 possible visits. All 83 of the participants met these criteria for inclusion in these analyses.

To assess the possible mediation pathways in Fig. 1 separate regression models in which RNT, depressive symptoms, anxiety, perceived stress, and BMI, predict IL-6 at each visit were examined. Furthermore, combinations of depressive symptoms, anxiety, perceived stress, with BMI were tested as mediators of the association between RNT and IL-6 at each visit in a series of regressions. In order to assess the possible mediation pathways in Fig. 2 separate regression models in which RNT, depressive symptoms, anxiety, and perceived stress predict breastfeeding duration were examined. Furthermore, combinations of depressive symptoms, anxiety, perceived stress, with BMI were tested as mediators of the association between RNT and breastfeeding duration in a series of regressions. In limited research, maternal age has been suggested to impact both BMI and IL-6 production (Zembala-Szczerba et al., 2017), maternal age was entered as a control variable during all mediation analyses. A 95 % confidence interval for unstandardized indirect effects for each visit was derived from using 10,000 bootstrapped samples using PROCESS (Hayes, 2017). SPSS 26 (IBM Corp., 2019) was used for all analyses.

3. Results

The study sample consisted of women 19–38 years old (M = 29.6, SD = 4.5) who reported they had given birth between 0 and 6 times (M = 1.0, SD = 1.1; Table 1). The majority of participants were non-Hispanic White women (72.3 %). A little less than a third (30.1 %) had a family income of less than $50,000, 34.9 % between $50,000 and $99,999, and 34.9 % earned $100,000 or more. In regards to educational attainment, approximately 12.0 % of participants had a high school diploma or less, 19.3 % attended college or a technical school, 26.5 % completed a bachelor's degree, and 42.2 % had complete some graduate or professional school coursework. Scores on the PTQ (M = 19.39, SD = 12.31) were lower than seen in the primary validation studies (M = 28.14, SD = 13.23) which used a sample that included 23 % males, and 79 % female university students (Ehring et al., 2011). In the current study sample, PTQ scores did not differ by racial group (p = .90), parity (p = .86), income (p = .86), or education (p = .15). Similarly, PTQ scores were not correlated with maternal age (p = .88).

Table 1
Sample characteristics.

	n	(%)	M	(SD)
Age			28.5	(4.6)
<25	15	(18.1 %)		
25 to 29	28	(33.7 %)		
30 to 34	31	(37.3 %)		
35–40	9	(10.8 %)		
Parity				
0	32	(38.6 %)		
1	36	(43.4 %)		
≥2	15	(18.1 %)		
Race				
White/Caucasian	60	(72.3 %)		
Black/African American	17	(20.5 %)		
Other	6	(7.2 %)		
Family income				
<$15,000	8	(9.6 %)		
$15,000–$29,999	6	(7.2 %)		
$30,000–$49,999	11	(13.3 %)		
$50,000–$74,999	16	(19.3 %)		
$75,000–$99,999	13	(15.7 %)		
≥$100,000	29	(34.9 %)		
Education				
Some high school	3	(3.6 %)		
High school graduate	7	(8.4 %)		
Some college (2-year college or technical school)	8	(9.6 %)		
Some college (4-year college)	4	(4.8 %)		
Associate's or technical degree	4	(4.8 %)		
Bachelor's degree	22	(26.5 %)		
Some graduate school or higher	35	(42.2 %)		

3.1. Inflammation results

3.1.1. Repetitive negative thinking

RNT, per PTQ scores, was associated with serum IL-6. This was seen in positive correlations between RNT and serum IL-6 during the third trimester (r = 0.224, p = .045), 4–6 weeks postpartum (r = 0.276, p = .02), and 8 months postpartum (r = 0.287, p = .02). Similarly, a trend towards a positive correlation was also observed at 4 months postpartum (r = 0.213, p = .076). This association was not statistically significant at 12 months postpartum (p = .13). A pathway by which RNT partially influences inflammation is through BMI. In this cohort, RNT was positively correlated with both BMI and serum IL-6 (Table 3 and Supplementary Fig. 4a). Further mediation analyses (Fig. 3a–e) demonstrated a consistent indirect effect of PTQ through BMI on IL-6 (β = 0.182 to 0.284) with significant bootstrapped unstandardized indirect effects at each timepoint (Visit 1: β = 0.0076, CI = 0.0028 to 0.0138; Visit 2: β = 0.0122, CI = 0.0060 to 0.0212; Visit 3: β = 0.0137, CI = 0.0061 to

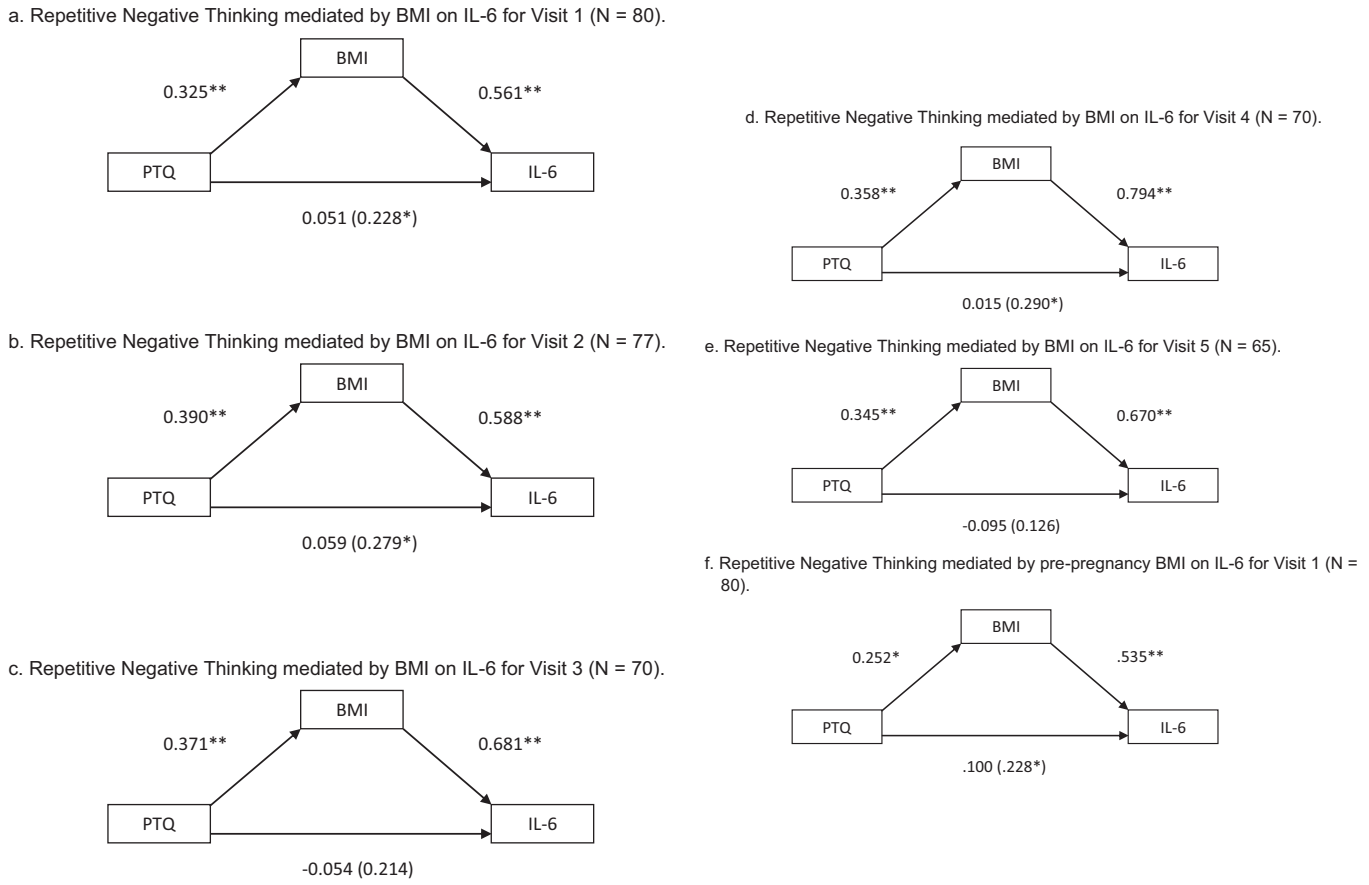

Fig. 3. a. Repetitive negative thinking mediated by BMI on IL-6 for Visit 1 (N = 80).
Note. *$p < .05$, **$p < .01$. PTQ to BMI $p = .002$, BMI to IL-6 $p < .001$, PTQ to IL-6 $p = .04$, PTQ to IL-6 with BMI in the model $p = .61$. Standardized indirect effect $\beta = 0.182$. Bootstrapped unstandardized indirect effect $\beta = 0.0076$, CI = 0.0028 to 0.0138.
b. Repetitive negative thinking mediated by BMI on IL-6 for Visit 2 (N = 77).
Note. *$p < .05$, **$p < .01$. PTQ to BMI $p < .001$, BMI to IL-6 $p < .001$, PTQ to IL-6 $p = .01$, PTQ to IL-6 with BMI in the model $p = .57$. Standardized indirect effect $\beta = 0.229$. Bootstrapped unstandardized indirect effect $\beta = 0.0122$, CI = 0.0060 to 0.0212.
c. Repetitive negative thinking mediated by BMI on IL-6 for Visit 3 (N = 70).
Note. *$p < .05$, **$p < .01$. PTQ to BMI $p \leq .001$, BMI to IL-6 $p < .001$, PTQ to IL-6 $p = .08$, PTQ to IL-6 with BMI in the model $p = .60$. Standardized indirect effect $\beta = 0.182$. Bootstrapped unstandardized indirect effect $\beta = 0.0137$, CI = 0.0061 to 0.0228.
d. Repetitive negative thinking mediated by BMI on IL-6 for Visit 4 (N = 70).
Note. *$p < .05$, **$p < .01$. PTQ to BMI $p = .002$, BMI to IL-6 $p < .001$, PTQ to IL-6 $p = .02$, PTQ to IL-6 with BMI in the model $p = .86$. The standardized indirect effect is $\beta = 0.284$. Bootstrapped unstandardized indirect effect $\beta = 0.0154$, CI = 0.0063 to 0.0252.
e. Repetitive negative thinking mediated by BMI on IL-6 for Visit 5 (N = 65).
Note. *$p < .05$, **$p < .01$. PTQ to BMI $p = .003$, BMI to IL-6 $p < .001$, PTQ to IL-6 $p = .32$, PTQ to IL-6 with BMI in the model $p = .36$. The Standardized indirect effect is $\beta = 0.231$. Bootstrapped unstandardized indirect effect $\beta = 0.0138$, CI = 0.0039 to 0.0251.
f. Repetitive negative thinking mediated by pre-pregnancy BMI on IL-6 for Visit 1 (N = 80).
Note. *$p < .05$, **$p < .01$. PTQ to BMI $p = .019$, BMI to IL-6 $p < .001$, PTQ to IL-6 $p = .04$, PTQ to IL-6 with BMI in the model $p = .32$. Standardized indirect effect $\beta = 0.073$. Bootstrapped unstandardized indirect effect $\beta = 0.0055$, CI = 0.0013 to 0.0112.

0.0228; Visit 4: $\beta = 0.0154$, CI = 0.0063 to 0.0252; Visit 5: $\beta = 0.0138$, CI = 0.0039 to 0.0251). Maternal age was not a significant contributor in the model for at any visit ($ps = .09$ to .82).

Additionally, research has suggested that pre-pregnancy BMI may be more relevant in predicting inflammation during pregnancy than BMI calculated from weights during pregnancy (e.g., Siddiqui et al., 2019). Similar to results using pregnancy-weight derived BMI, there was an association between RNT and inflammation during pregnancy, through pre-pregnancy BMI with a standardized indirect effect $\beta = 0.073$, and a significant bootstrapped unstandardized indirect effect $\beta = 0.0055$, CI = 0.0013 to 0.0112 (Fig. 3f). Maternal age was not a significant contributor to this model ($p = .09$).

3.1.2. Repetitive negative thinking and depressive symptoms

RNT was positively correlated with depressive symptoms, per QIDS scores, at each study Visit ($rs = 0.406$ to 0.613, $ps \leq .001$; Table 2 and Supplementary Fig. 1a). Greater RNT predicted greater depressive symptoms across the entire assessment period, as evidenced by a significant main effect of PTQ on QIDS scores ($F(36,78.294) = 4.276$, $p < .001$; Table 5). Depressive symptoms were greater during late pregnancy and 4–6 weeks postpartum than at later Visits during the study, demonstrated by a main effect of Visit timing on QIDS scores ($F(4,73.711) = 11.298$, $p < .001$). For women with higher RNT, depressive symptoms were highest during pregnancy decreasing over the study period, while women with lower RNT had the least depressive symptoms during pregnancy which increased into postpartum. Over the study period depressive symptoms of women with lower-than-average RNT tended to remain below that of participants with higher-than-average RNT. These patterns were supported by a significant interaction between PTQ score and Visit timing ($F(137,76.994) = 2.139$, $p < .001$;

Table 2
Correlations between study variables part 1 of 2.

	Age	PTQ	QIDS					CUXOS					PSS				
			Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
PTQ	0.018																
QIDS																	
Visit 1	0.066	0.628															
Visit 2	0.163	0.374	0.367														
Visit 3	0.073	0.404	0.331	0.481													
Visit 4	0.253	0.501	0.418	0.553	0.581												
Visit 5	0.226	0.473	0.411	0.474	0.425	0.635											
CUXOS																	
Visit 1	0.243	0.707	0.564	0.388	0.253	0.446	0.354										
Visit 2	0.133	0.543	0.398	0.534	0.394	0.549	0.371	0.540									
Visit 3	0.076	0.423	0.338	0.468	0.658	0.564	0.236	0.435	0.679								
Visit 4	0.220	0.578	0.407	0.478	0.510	0.722	0.438	0.633	0.732	0.777							
Visit 5	0.339	0.559	0.373	0.335	0.385	0.603	0.605	0.581	0.564	0.494	0.632						
PSS																	
Visit 1	0.105	0.677	0.546	0.397	0.257	0.442	0.504	0.669	0.378	0.291	0.499	0.532					
Visit 2	0.042	0.461	0.354	0.568	0.273	0.400	0.296	0.428	0.571	0.458	0.512	0.338	0.680				
Visit 3	0.102	0.496	0.305	0.388	0.633	0.527	0.305	0.373	0.464	0.694	0.589	0.432	0.567	0.578			
Visit 4	0.115	0.508	0.292	0.500	0.432	0.612	0.484	0.434	0.501	0.588	0.702	0.513	0.654	0.673	0.711		
Visit 5	0.132	0.446	0.233	0.465	0.385	0.607	0.713	0.336	0.398	0.367	0.532	0.642	0.616	0.574	0.560	0.741	
BMI																	
Visit 0	0.298	0.247	0.107	0.081	0.158	0.175	0.113	0.046	0.035	0.010	0.077	0.028	0.249	0.182	0.186	0.167	0.134
Visit 1	0.261	0.320	0.139	0.118	0.168	0.245	0.131	0.142	0.109	0.022	0.148	0.038	0.301	0.252	0.214	0.222	0.156
Visit 2	0.237	0.384	0.177	0.106	0.158	0.255	0.136	0.225	0.131	0.045	0.198	0.063	0.359	0.275	0.233	0.247	0.163
Visit 3	0.227	0.369	0.184	0.108	0.153	0.203	0.086	0.207	0.147	0.070	0.175	0.022	0.352	0.291	0.253	0.235	0.095
Visit 4	0.225	0.352	0.162	0.146	0.118	0.268	0.146	0.227	0.185	0.079	0.221	0.053	0.355	0.299	0.271	0.277	0.173
Visit 5	0.247	0.333	0.156	0.169	0.125	0.272	0.174	0.166	0.202	0.051	0.208	0.072	0.347	0.290	0.254	0.250	0.202
IL-6																	
Visit 1	0.185	0.224	0.152	0.269	0.040	0.261	0.106	0.150	0.285	0.126	0.258	0.080	0.198	0.268	0.177	0.163	0.128
Visit 2	0.116	0.276	0.308	0.188	0.088	0.239	0.135	0.153	0.194	0.125	0.242	0.086	0.184	0.225	0.211	0.206	0.066
Visit 3	0.039	0.213	0.169	0.030	0.050	0.120	0.047	0.174	0.115	0.064	0.110	0.064	0.196	0.129	0.185	0.132	0.007
Visit 4	0.090	0.287	0.185	0.139	0.123	0.241	0.156	0.269	0.154	0.100	0.250	0.089	0.316	0.248	0.238	0.230	0.170
Visit 5	0.025	0.125	0.105	0.123	0.037	0.086	0.053	0.129	0.062	0.083	0.035	0.083	0.211	0.106	0.123	0.060	0.047
BFD	0.103	0.244	0.083	0.035	0.178	0.218	0.295	0.236	0.179	0.208	0.177	0.151	0.290	0.139	0.353	0.349	0.247

Note. *$p < .05$, **$p < .01$. Visit 1, N = 83, Visit 2, N = 79, Visit 3, N = 73, Visit 4, N = 73, Visit 5, N = 69. BFD = breastfeeding duration in weeks, N = 72.

Supplementary Fig. 1b). Depressive symptoms did not mediate the association between RNT and inflammation, as bootstrapped models which included BMI as a covariate failed to reach significance (95 % CIs included 0).

3.1.3. Repetitive negative thinking and anxiety symptoms

Similar to the patterns of association seen with depressive symptoms, RNT was positively correlated with anxiety symptoms, per CUXOS scores, at each study Visit ($rs = 0.442$ to 0.655, $ps < .001$; Table 2 and Supplementary Fig. 2a). Greater RNT predicted more anxiety symptoms across the study period, as evidenced by a main effect of PTQ scores ($F(36,78.030) = 3.579$, $p < .001$; Table 6). Anxiety symptoms were highest during pregnancy and declined during the postpartum year, which is reflected by a main effect of Visit timing ($F(4,74.575) = 13.395$, $p < .001$). There was also an interaction between PTQ scores and Visit timing, such that while women with higher-than-average RNT tended to have more anxiety symptoms, the difference between those with higher-than-average and lower-than-average RNT attenuated through the first year ($F(137,75.518) = 1.853$, $p = .002$; Supplementary Fig. 2b). The prominent difference in anxiety between those with higher-than-average versus lower-than-average RNT during pregnancy is attenuated during postpartum. Anxiety did not mediate the association between RNT and inflammation, as bootstrapped models which included BMI as a covariate failed to reach significance (95 % CI included 0).

3.1.4. Repetitive negative thinking and perceived stress

RNT was positively correlated with perceived stress (per PSS scores) at each study Visit ($rs = 0.448$ to 0.656, $ps < .001$; Table 2, Supplementary Fig. 3a). Women with higher-than-average RNT tended to have more perceived stress than those with lower-than-average RNT, demonstrated by a main effect of PTQ scores ($F(36,77.504) = 3.765$, $p < .001$; Table 7). These differences were greater during pregnancy and attenuated during postpartum, as evidenced by an interaction between PTQ scores and Visit in predicting perceived stress ($F(137,75.552) = 1.999$, $p < .001$; Supplementary Fig. 3b). However, unlike the pattern of changes between Visits seen with depressive and anxiety symptoms over the course of the study period, there was not a main effect of Visit on PSS scores ($p = .09$). Perceived stress was not a mediator between RNT and inflammation as bootstrapped models which included BMI as a covariate failed to reach significance (95 % CI included 0).

3.2. Breastfeeding duration results

3.2.1. Repetitive negative thinking

Repetitive negative thinking was negatively associated with total weeks of breastfeeding duration ($r = -0.244$, $p = .04$; Table 2, Supplementary Fig. 5a). Those with lower RNT tended to breastfeed longer. Women who continued to breastfeed for 6 months or more had lower RNT (M = 16.22, SD = 11.00) compared to those who breastfed for <6 months or never breastfed (M = 23.65, SD = 13.01; $t(70) = -2.578$, $p = .01$; Supplementary Fig. 5b).

Table 4
Fit indices across models.

Dependent variable	Model	R matrix	AIC	BIC
QIDS	A	Unstructured	1774.795	1857.372
	B	Compound symmetry	1768.997	1800.455
	C	First-order autoregressive	1767.198	1798.656
	D	Heterogeneous first-order autoregressive	1771.319	1818.506
CUXOS	A	Unstructured	2587.469	2670.046
	B	Compound symmetry	2597.775	2629.233
	C	First-order autoregressive	2600.459	2631.917
	D	Heterogeneous first-order autoregressive	2604.184	2651.371
PSS	A	Unstructured	2195.778	2278.355
	B	Compound symmetry	2191.631	2223.089
	C	First-order autoregressive	2202.565	2234.023
	D	Heterogeneous first-order autoregressive	2207.361	2254.547

Note: Model A was used in each case as other models did not significantly improve AIC.

3.2.2. Repetitive negative thinking and depressive symptoms

More depressive symptoms at 1 year postpartum were associated with fewer weeks of breastfeeding as seen with the correlation between QIDS scores and breastfeeding duration in weeks ($r = -0.295$, $p = .02$), but not at other visits ($rs = -0.035$ to -0.218, $ps = 0.08$ to 0.77; Table 2). Depressive symptoms at each visit did not mediate the association between RNT and breastfeeding duration, as the mediation analyses for each visit did not meet the criteria for significance during bootstrapping (95 % CI included 0).

3.2.3. Repetitive negative thinking and anxiety

Greater anxiety during pregnancy was associated with fewer weeks of breastfeeding, as seen in the correlation between CUXOS scores and breastfeeding duration ($r = -0.236$, $p = .05$) but not for any other visit ($rs = -0.151$ to -0.208, $ps = 0.09$ to 0.243; Table 2). Anxiety at each visit did not mediate the association between RNT and breastfeeding duration, as the mediation analyses for each visit did not meet the criteria for significance during bootstrapping (95 % CI included 0).

3.2.4. Repetitive negative thinking and perceived stress

Higher perceived stress was associated with fewer weeks of breastfeeding, as supported by negative correlations during pregnancy ($r = -0.290$, $p = .02$), at 4 months postpartum ($r = -0.353$, $p = .004$), 8

Table 3
Correlations between study variables part 2 of 2.

	BMI						IL-6				
	Visit 0	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
BMI											
Visit 1	0.946										
Visit 2	0.925	0.981									
Visit 3	0.921	0.961	0.984								
Visit 4	0.924	0.953	0.964	0.989							
Visit 5	0.937	0.954	0.954	0.977	0.990						
IL-6											
Visit 1	0.542	0.571	0.558	0.662	0.684	0.680					
Visit 2	0.512	0.573	0.582	0.648	0.663	0.635	0.657				
Visit 3	0.629	0.629	0.647	0.653	0.650	0.644	0.654	0.692			
Visit 4	0.719	0.715	0.752	0.757	0.776	0.771	0.678	0.667	0.667		
Visit 5	0.557	0.558	0.582	0.605	0.614	0.626	0.560	0.582	0.717	0.593	
BFD	0.083	0.105	0.130	0.167	0.188	0.158	0.095	0.173	0.295	0.159	0.086

Note. *$p < .05$, **$p < .01$.Visit 1, N = 83, Visit 2, N = 79, Visit 3, N = 73, Visit 4, N = 73, Visit 5, N = 69. BFD = breastfeeding duration in weeks, N = 72.

Table 5
Depressive symptoms estimates of fixed effects by repetitive negative thinking at visit.

Parameter	Estimate	SE	*df*	*t*	*p*	95 % CI	
Intercept	3.399	0.350	81.892	9.711	0.000	2.703	4.095
RNT	0.093	0.020	113.445	4.683	0.000	0.053	0.132
3rd trimester	0.059	0.017	77.417	3.428	0.001	0.025	0.094
4–6 weeks	0.042	0.017	73.621	2.460	0.016	0.008	0.075
4 months	0.005	0.017	74.288	0.324	0.747	0.028	0.039
8 months	0.004	0.014	70.326	0.284	0.778	0.024	0.032

Note. Greater depressive symptoms were predicted by RNT, had a higher average during pregnancy decreasing across postpartum, and differences between those with higher-than-average and lower-than-average RNT attenuated over time (Supplementary Fig. 1b). This is seen with a main effect of RNT ($F(36,78.29) = 4.28$, $p < .001$), a main effect of visit ($F(4,73.71) = 11.30$, $p < .001$) and an interaction between RNT and visit timing ($F(137,76.99) = 2.14$, $p < .001$).

Table 6
Anxiety symptoms estimates of fixed effects by repetitive negative thinking at visit.

Parameter	Estimate	SE	*df*	*t*	*p*	95 % CI	
Intercept	4.231	1.254	74.792	3.374	0.001	1.733	6.728
RNT	0.369	0.062	95.776	5.964	0.000	0.246	0.492
3rd trimester	0.312	0.050	69.092	6.236	0.000	0.212	0.412
4–6 weeks	0.030	0.046	73.137	0.665	0.508	0.061	0.122
4 months	0.013	0.046	72.475	0.281	0.780	0.106	0.080
8 months	0.049	0.044	71.616	1.113	0.270	0.038	0.136

Note. Greater anxiety symptoms were predicted by RNT, had a higher average during pregnancy decreasing across postpartum, and differences between those with higher-than-average and lower-than-average RNT attenuated over time (Supplementary Fig. 2b). This is seen with a main effect of RNT ($F(36,78.03) = 3.58$, $p < .001$), a main effect of visit ($F(4,74.58) = 13.40$, $p < .001$) and an interaction between RNT and visit timing ($F(137,75.52) = 1.853$, $p = .002$).

Table 7
Perceived stress estimates of fixed effects by repetitive negative thinking at visit.

Parameter	Estimate	SE	*df*	*t*	*p*	95 % CI	
Intercept	3.399	0.350	81.892	9.711	0.000	2.703	4.095
RNT	0.093	0.020	113.445	4.683	0.000	0.053	0.132
3rd trimester	0.059	0.017	77.417	3.428	0.001	0.025	0.094
4–6 weeks	0.042	0.017	73.621	2.460	0.016	0.008	0.075
4 months	0.005	0.017	74.288	0.324	0.747	0.028	0.039
8 months	0.004	0.014	70.326	0.284	0.778	0.024	0.032

Note. Greater perceived stress was predicted by RNT, and differences between those with higher-than-average and lower-than-average RNT attenuated over time (Supplementary Fig. 3b). This is seen with a main effect of RNT ($F(36,77.50) = 3.77$, $p < .001$), and an interaction between RNT and visit timing ($F(137,75.55) = 2.00$, $p = .001$).

months postpartum ($r = 0.349$, $p = .004$), and marginally at 1 year postpartum ($r = 0.247$, $p = .053$). However, the association between perceived stress at 4–6 weeks postpartum and breastfeeding duration was not significant ($r = 0.139$, $p = .25$; Table 2). Perceived stress at each visit, did not mediate the association between RNT and breastfeeding duration, as the mediation analyses for each visit did not meet the criteria for significance during bootstrapping (95 % CI included 0).

4. Conclusions

In this cohort of perinatal women assessed from late pregnancy through one year postpartum, repetitive negative thinking (RNT) was positively associated with symptoms of depression, anxiety, and stress through one year postpartum, as well as inflammation in late pregnancy through 8 months postpartum. The association between RNT and inflammation was partially mediated by BMI which suggests a pathway through which RNT influences IL-6. Furthermore, RNT was negatively associated with breastfeeding duration. Specifically, those breastfeeding <6 months, the recommended time for exclusive breastfeeding by the American Academy of Pediatrics (Eidelman and Schanler, 2012), reported greater RNT. While RNT was associated with depressive symptoms, anxiety, and perceived stress during pregnancy and postpartum, mental health indicators did not serve as a pathway by which RNT was associated with IL-6 or breastfeeding duration. Together these findings partially support the relationships set out in the hypotheses and suggest that RNT has adverse consequences for maternal and child health. Characterized by unique motivations as well as health consequences, pregnancy and postpartum represent an opportunity for intervention to reduce RNT with potential for multi-faceted and long-term benefits.

In this study, as hypothesized, RNT was positively associated depressive symptoms. The strongest correlation (indicative of a large effect size) and the greatest differences in depressive symptoms between above and below average RNT groups were seen during pregnancy. While prior research on RNT and perinatal depression has been limited, there are conflicting findings in the literature with some studies finding that RNT measured at 2 months postpartum does (Barnum et al., 2013) or does not (Müller et al., 2013a) predict postpartum depressive symptoms. These differences in prior findings may be due to heightened variations of intrapersonal characteristics such as perfectionism (e.g., Egan et al., 2017) or interpersonal characteristics such as social functioning (e.g., O'Mahen et al., 2010) which may impact overall mental health during postpartum. However, our findings are similar to those seen in literature where RNT is associated with depressive symptoms (Raes, 2012). These associations were also similar to the results of a study by Schmidt et al. (2017), in which maternal RNT at 4 months was positively associated with postpartum depressive symptoms, and negatively associated with self-reported bonding with one's infant. The benefits of lower RNT may impart themselves not only onto maternal mental health but may also improve the quality of the relationship a new mother develops with their infant.

Our findings regarding RNT and symptoms of anxiety are consistent with prior research on RNT specific to pregnancy, in which pregnant

women with an anxiety-related mental health diagnosis (e.g., Generalized Anxiety Disorder) had higher PTQ scores than those without a diagnosis (Atadokht et al., 2020). Similar to our findings with depression, the positive association between RNT and anxiety was strongest, with a large effect size, during pregnancy, with those with higher-than-average RNT having the most symptoms of anxiety during pregnancy. While these differences between higher- and lower-than-average groups attenuated during postpartum, the association remained strong, suggesting a continuing influence of RNT on anxiety through the first year. The impact of pregnancy-specific anxiety may account for some of this heightened effect during pregnancy (Huizink et al., 2014) and should be considered in future research.

The association between stress and adverse pregnancy outcomes is complex, as health effects can be dependent on the timing and duration of a stressor (Glynn et al., 2008; Hilmert et al., 2016; Strahm et al., 2020). The positive association between RNT and perceived stress during pregnancy had a large effect size and was the strongest of any Visit during the study period, and the differences between higher- and lower-than-average RNT was the largest. However, similar to depression and anxiety, these effects were reduced postpartum. Further clarification is needed on whether interventions for RNT can reduce the impact of perceived stress, and thus reduce the consequences of stress (e.g., depressive and anxiety symptoms) as they occur during pregnancy and postpartum.

The relationship between RNT and inflammation, through which RNT's effect on IL-6 was through BMI's influence on IL-6 production, was supported by other research on BMI and IL-6 production during pregnancy (Christian and Porter, 2014; Siddiqui et al., 2019) and consistent with prior results reported by our lab using a different perinatal sample (Mitchell and Christian, 2019). These relationships between RNT, BMI, and IL-6 suggest that reducing RNT may have peripheral benefits to supporting a lower BMI as part of minimizing RNT related inflammation. Mental health indicators did not mediate the association between RNT and inflammation, suggesting that RNT may have a distinct relationship with inflammation. However further research is necessary to parse out the role of possible biobehavioral pathways that explain the relationship between RNT and BMI, such as the role of RNT in relation to disordered eating behaviors (Kornacka et al., 2020; Sala et al., 2019) which may have heightened influence due to cravings during pregnancy (e.g., Blau et al., 2018).

Additionally, breastfeeding duration was negatively associated with RNT in our study. In other research, breastfeeding duration is negatively associated with symptoms of anxiety and depression (Dias and Figueiredo, 2015; Grigoriadis et al., 2013; Ritchie-Ewing et al., 2019). Mental health indicators did not mediate the association between RNT and breastfeeding duration, suggesting that RNT may have a distinct relationship with breastfeeding. While many factors not included in the current analyses influence breastfeeding duration (Cohen et al., 2018; Santana et al., 2018), reducing the influence of higher RNT may influence breastfeeding through additional paths we were not able to account for here, such as attendance in breastfeeding classes (a related health behavior). Further research is warranted on the association between RNT and factors known to affect likelihood and duration of breastfeeding. It is possible that reducing RNT during pregnancy could have an overall salubrious effect through multiple pathways, which may increase breastfeeding duration.

As a transdiagnostic characteristic RNT provides an opportunity to reduce the severity of the symptoms of depression and anxiety, as well as perceived stress during pregnancy through the first year postpartum. The results of this study provide novel insight into the associations between maternal RNT, symptoms of depression, anxiety and stress, inflammation, and breastfeeding during late pregnancy through the first year postpartum. Together with prior research they suggest that there are likely benefits for mothers and infants for providing interventions to reduce RNT. Further research on role of RNT in pregnancy and postpartum outcomes, as well as the application of interventions to reduce RNT is indicated.

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Declaration of competing interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2022.09.067.

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