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Increased blood serotonin concentrations are correlated with reduced tension/anxiety in healthy postpartum lactating women

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Abstract

The serotonin (5-HT) system in the brain plays an important role in mood regulation. The postpartum period is considered a high-risk time for mood and anxiety disorders. We assessed changes in 5-HT levels in whole blood (as an indicator of brain 5-HT concentrations) and mood states before and after delivery in 28 healthy, lactating postpartum women. Mood states were evaluated using Profile of Mood States questionnaires (POMS). Measurements were done on the same day in early (first week) and late (third–fourth and sixth–seventh weeks) postpartum, and compared with those in the third trimester and in age-matched, healthy, non-pregnant women. Mean 5-HT concentrations were significantly higher and mean tension/anxiety scores of POMS were significantly lower in late (but not early) postpartum than in the third trimester or non-pregnant controls. 5-HT concentrations correlated with tension/anxiety in the third trimester and late postpartum, indicating an important role for the 5-HT system in the regulation of tension/anxiety in healthy postpartum women. The mechanism underlying the changes in the 5-HT system may be rapid inhibition induced by the marked decrease in estradiol after delivery and gradual excitation caused by lactation-induced brain oxytocin release during the postpartum period.

Keywords

Estradiol; Oxytocin; Mood

1. Introduction

Serotonin (5-HT) is an important neurotransmitter in the central nervous system that has been implicated in the regulation of mood. Because of its anxiolytic and anti-depressive effects, selective serotonin reuptake inhibitors (SSRIs) have been used for treatment of both major depression and postpartum depression (Appleby et al., 1997; Misri et al., 2004). It is thus reasonable to hypothesize that 5-HT in the brain may be linked to mood changes during postpartum.

The postpartum period is considered to be a high-risk time for mood and anxiety disorders (Cox et al., 1993; Seyfried and Marcus, 2003). During the first week postpartum, approximately 15% of Japanese women experience 'postpartum blues', which are characterized by transient mood changes (Murata et al., 1998).

It is important to note that most women with postpartum blues recover quickly without any treatment (Kennerley and Gath, 1986). The mechanisms underlying such transient mood changes during the postpartum period have not been fully evaluated. We conducted the present study to assess the relationship between mood states and 5-HT levels in the blood (as an indicator of brain 5-HT concentrations) during the postpartum period in healthy lactating women.

Since a transient negative mood change occurs during the first week after

delivery, the postpartum period in this study was divided into early postpartum (first week postpartum) and late postpartum (third–fourth and sixth–seventh week postpartum).

The aim of this study was to evaluate mood states in healthy, lactating postpartum women without postpartum depression and/or blues. We thus did not administer any specific psychological tests commonly used to diagnose the disorder. However, Profile of Mood States (POMS) questionnaires (McNair and Heuchert, 2003) are specifically designed for repeated measurement in healthy subjects. In fact, several clinical reports have used POMS questionnaires to assess mood states in healthy women during the postpartum period (Buckwalter et al., 1999; Nasta et al., 2002). Therefore, we used POMS questionnaires in this study.

To estimate changes in 5-HT levels in the brain, we analyzed 5-HT concentrations in whole blood. The rationale for this approach has been demonstrated by a previous *in vivo* experiment, in which we showed that augmented 5-HT within the brain crosses the blood–brain barrier via a 5-HT transporter (Nakatani et al., 2008). Because blood platelets quickly take up 5-HT released from the brain into the systemic circulation (Pletscher, 1987), augmentation of 5-HT in the blood may be expected to be manifested in both the

plasma and platelets. We therefore measured 5-HT concentrations in whole blood.

Mood states and WB 5-HT concentrations during early and late postpartum were compared with those before delivery (in the third trimester of pregnancy) and those in age-matched, healthy, non-pregnant women.

To explore the mechanisms underlying transient mood changes during the postpartum period, we focused on estradiol and oxytocin, two biological factors affecting the activity of the 5-HT system in the brain. The activity of the 5-HT system in the brain is influenced by estradiol through the inhibition of monoamine oxidase A (MAO-A) (Smith et al., 2004), which is known to promote 5-HT degradation (Bethea et al., 2002). A marked decrease in estradiol after delivery may cause disinhibition or activation of MAO-A, which may induce increased 5-HT degradation, and therefore decreased 5-HT activity in the brain, during the postpartum period.

Oxytocin (OXT) regulates milk ejection when released into the blood during lactation (Lincoln and Paisley, 1982). A microdialysis study by Neumann et al. (1993) showed that OXT levels in the brain increase during lactation, and it has recently been shown that OXT plays a significant role in the hyporesponsiveness of the maternal brain to stress (Slattery and Neumann, 2008). A recent study by Yoshida et al. (2009) demonstrated that OXT has an anxiolytic effect in mice,

which is exerted via OXT receptors expressed on 5-HT neurons. It is thus likely that OXT is one of the excitatory factors influencing the 5-HT system in the brain during the postpartum period.

All postpartum women in this study continued to breastfeed throughout the evaluation period. According to the report by Johnston and Amico (1986), basal plasma OXT level is not different in breastfeeding and non-breastfeeding women. OXT increases significantly in response to infant suckling. The OXT release is dependent upon nipple stimulation. Lactation-induced OXT release disappears quickly after stopping breastfeeding. Thus, blood sampling was required to conduct shortly after infant suckling. This experimental procedure was possible only while the subject remained in the maternity ward. Therefore, only a small portion of postpartum breastfeeding women participated in this experiment.

2. Material and methods

2.1. *Participants*

Twenty-eight healthy women in the third trimester of pregnancy (postpartum group; mean age 33.1 ± 4.4 years, range 21–41 years) were recruited from a private maternity hospital in Tokyo. All women had normal pregnancies and vaginal deliveries; eight women were primiparous and 20 were multiparous. Postpartum, all women breastfed and continued to breastfeed throughout the period of evaluation.

For the evaluation of WB 5-HT concentrations and mood states, 28 age-matched, healthy, non-pregnant women (non-pregnant control group; mean age 33.2 ± 5.0 years, range 24–43 years) were recruited as a control group. Our previous study (Kikuchi et al., 2010) showed no significant differences in either WB 5-HT concentration or POMS score between the follicular and premenstrual phase in healthy women. We therefore did not limit our evaluations to any specific phase of the menstrual cycle in the non-pregnant women.

All postpartum and non-pregnant control women in this study were nonsmokers and had no history of psychiatric illnesses, neurotoxin use or head injuries. All women gave informed consent and were informed that they were free to stop participating in the study at any time. The study and recruitment

procedures were approved by the Ethics Committee of Toho University School of Medicine and conducted in accordance with the Declaration of Helsinki.

2.2. *Experimental protocol*

The transient negative mood change commonly occurs during the first week after delivery. Therefore, we divided the postpartum period into an early and two late postpartum periods. The early postpartum period was defined as the first week (days 1–6) after delivery and the late postpartum periods consisted of the third and fourth week (days 19–25), and sixth and seventh week (days 36–47) after delivery. Control measurements were performed in the third trimester (33–40 weeks of gestation). Thus, there were four assessment sessions: third trimester, first week postpartum, third–fourth week postpartum and sixth–seventh week postpartum.

In the postpartum group, 4.5 mL of blood was drawn in two Vacutainer tubes during the four assessment sessions; 0.5 mL for 5-HT measurement and 4.0 mL for estradiol measurement. The POMS questionnaire was performed at the same time.

For analysis of 5-HT, 0.5 mL blood was collected in a Vacutainer tube containing heparin sodium salt and diluted with 2.5 mL water. Next, 30 μL of the

internal standard and 10 μL of a 10% (weight per volume) solution of ascorbic acid in water were added to the diluted blood sample. The samples were then stored at −20°C until assay.

For estradiol measurements, 4 mL blood in a Vacutainer tube was centrifuged and stored at −20°C until assay.

To estimate the increase in OXT concentration in the brain induced by infant suckling, we measured plasma OXT concentrations in 12 women who were still in the maternity ward, and from whom we were able to draw blood shortly (5–30 min) after breastfeeding. In these women, an additional 3.5 mL blood sample for measurement of plasma OXT concentration was taken at the time of blood sampling for 5-HT and estradiol measurements in the first week postpartum.

The blood samples for OXT were collected in ice-chilled tubes containing EDTA-2NA, orthophenanthroline and sodium citrate to prevent the destruction of OXT by oxytocinase. The tubes were placed in an ice bath and centrifuged at 4°C (3000 rpm, 10 min). The plasma was stored at −20°C until assay.

In the non-pregnant control group, a single blood sample was taken for 5-HT measurement and a single POMS questionnaire was administered.

2.3. *Biochemical analyses*

WB 5-HT was analyzed using methods described in detail by Kremer et al. (1990) and Mohri et al. (2005). High-performance liquid chromatography (HPLC) analysis was performed within 3 weeks of obtaining the samples. The blood samples were thawed and 167 μL methanol was added to 1 mL blood to remove proteins. The samples were then centrifuged at 4670 *g* for 10 min at 4°C. Of the supernatants, 500 μL was suspended in 4.5 mL mobile phase buffer. The mobile phase consisted of a phosphate buffer (Na^+, 0.1 M) containing 50 mg/L ethylenediaminetetra-acetic acid-2Na and ion-pair (300 mg/L sodium-octyl-sulfate, Nacalai Tesque, Kyoto, Japan) and 20% methanol at pH 6.0.

5-HT concentrations were determined using an HPLC-electrochemical detection system (Eicom 300, Eicom, Kyoto, Japan). The working electrode was a graphite carbon electrode set at a detector potential of +400 mV against an $Ag/AgCl_2$ reference electrode. 5-HT was separated on a reversed-phase column (Eicompak CA-5 ODS, Eicom, Kyoto, Japan). The flow rate was set at 0.27 mL/min and the analysis temperature was 35°C.

Serum estradiol concentrations were measured using an electrochemiluminescence immunoassay analyzer with an Elecsys Systems kit (Estradiol II; Roche Diagnostics, Tokyo, Japan). The detection limit was 10 pg/mL.

OXT was analyzed using the method described in detail by Mizutani et al. (1982). The plasma sample for OXT measurement was heated at 56°C for 30 min to inactivate serum oxytocinase (Oya et al., 1974). After further centrifugation, the supernatant was analyzed for OXT by radioimmunoassay using a gamma counter (ARC1000, Aloca, Tokyo, Japan). The detection limit was 3.0 μU/mL.

2.4. *Psychological testing*

To assess the psychological mood, a POMS questionnaire (Buckwalter et al., 1999; Nasta et al., 2002) was completed for < 5 min on the same days as blood sampling at all four assessment times. The POMS questionnaire is widely used and standardized to assess mood profiles, and consists of 30 adjectives rated on a 5-point (0−4) scale (McNair and Heuchert, 2003). The adjective scores are combined to form six summary scores that measure one positive and five negative dimensions: vigor (positive), and tension/anxiety, depression/dejection, anger/hostility, fatigue, and confusion (negative). Reliability coefficients for internal consistency were reported as 0.90 in the manual accompanying the instrument (McNair et al., 1992), based on data from numerous validity studies and normative samples. POMS questionnaire was administered during specific periods in pregnancy and/or postpartum. Thus, internal consistency reliability

was confirmed by Cronbach's alpha coefficients with 0.70 or above viewed as adequate.

2.5. *Statistical analyses*

Mean changes over time in WB 5-HT and the subscales of POMS were analyzed by one-way repeated-measures analysis of variance (ANOVA) with time (third trimester, first, third–fourth and sixth–seventh weeks postpartum) as a within-subject factor in the postpartum group. Significant differences over time shown by ANOVA were further evaluated with Scheffe's *post-hoc* test. If significant mean changes over time were found in WB 5-HT or the subscales of POMS, student's unpaired *t*-tests were used to compare with the corresponding data obtained in the non-pregnant control group. For these statistical analyses, the level of significance was set at 0.05.

Correlations between WB 5-HT concentrations and the subscales of the POMS questionnaires in the postpartum group were examined using Spearman rank correlation coefficients with Bonferroni correction. Effects were considered to be statistically significant when the *p*-values were less than 0.0125 (0.05/4 comparisons).

All data are expressed as the mean ± standard deviation (SD).

3. Results

3.1. *Serotonin concentrations*

Figure 1 illustrates the changes in mean WB 5-HT concentrations in the postpartum group during the four assessment periods. Mean WB 5-HT concentrations were higher in the third–fourth (210.9 ± 71.1 ng/mL) and sixth–seventh weeks postpartum (202.1 ± 68.4 ng/mL) than in the third trimester (142.0 ± 50.7 ng/mL). There were no apparent changes in mean WB 5-HT concentrations between the third trimester and the first week postpartum (159.3 ± 58.7 ng/mL). One-way ANOVA revealed significant changes over time ($F_{3,81}$ = 20.6, $p < 0.0001$). *Post-hoc* tests showed that mean WB 5-HT concentrations were lower in the third trimester than in both the third–fourth ($p < 0.0001$) and sixth–seventh week postpartum ($p < 0.0001$). Mean WB 5-HT concentrations were also lower in the first week postpartum than in both the third–fourth ($p < 0.0001$) and sixth–seventh week postpartum ($p < 0.01$).

3.2. *Profile of Mood States scores*

Cronbach's alpha coefficients of the total score of POMS ranged from 0.72 to 0.82 for the four assessment sessions; 0.81 in the third trimester; 0.82 in the first week postpartum; 0.82 in the third–fourth week postpartum; and 0.72 in the

sixth–seventh week postpartum, all of which exceeded the acceptable level of 0.70. Cronbach's alpha coefficients of the POMS subscales in the four assessment sessions ranged from 0.72 to 0.94 for tension/anxiety, vigor and fatigue, while those of depression/dejection, anger/hostility and confusion had a reliability of less than 0.70. Thus, further statistical analyses were performed on three subscales of POMS in this study; tension/anxiety, vigor and fatigue.

Figure 2 shows the mean scores for tension/anxiety (A), vigor (B) and fatigue (C) of POMS questionnaire in the postpartum group at the times indicated.

Mean tension/anxiety scores were lower in the third–fourth and sixth–seventh weeks postpartum than in the third trimester, but there were no differences in mean tension/anxiety scores between the third trimester and the first week postpartum. One-way ANOVA revealed significant changes in tension/anxiety scores in the postpartum group over time ($F_{3,81}$= 6.4, $p < 0.001$). Mean tension/anxiety scores were higher in the third trimester than in the sixth–seventh week postpartum ($p < 0.05$), and higher in the first week postpartum than in both the third–fourth week ($p < 0.05$) and the sixth–seventh week postpartum ($p < 0.01$).

As for the mean vigor and fatigue scores, there were no changes over time, apart from a higher vigor score in the first week postpartum ($p < 0.05$) than in the

third–fourth week postpartum.

3.3. *Mean whole blood serotonin concentrations and mean tension/anxiety scores in the postpartum group and the non-pregnant control group*

Mean WB 5-HT concentration and mean tension/anxiety scores of POMS in the non-pregnant control group are shown as horizontal broken lines within gray boxes (SD) in Fig. 1 and Fig. 2-A, respectively.

Compared with the mean WB 5-HT concentration in the non-pregnant control group (159.2 ± 51.8 ng/mL), mean WB 5-HT concentrations were significantly higher in the postpartum group in the third–fourth (210.9 ± 71.1 ng/mL; $t_{54} = 3.1$, $p < 0.01$) and sixth–seventh week postpartum (202.1 ± 68.4 ng/mL; $t_{54} = 2.6$, $p < 0.01$). However, there were no significant differences in mean WB 5-TH concentrations between the non-pregnant control group and either the third trimester (142.0 ± 50.7 ng/mL) or the first week postpartum (159.3 ± 58.7 ng/mL).

Compared with the non-pregnant control group, mean tension/anxiety scores in the postpartum group were significantly lower in the third–fourth ($t_{54} = -2.6$, $p < 0.01$) and sixth–seventh weeks postpartum ($t_{54} = -3.2$, $p < 0.01$). No significant differences were found between the control group and the third

trimester and the first week postpartum in the postpartum group.

3.4. *Correlations between whole blood serotonin concentrations and tension/anxiety scores*

Figure 3 shows the correlations between WB 5-HT concentrations and tension/anxiety scores of individual subjects in (A) the third trimester, (B) the first, (C) third–fourth and (D) sixth–seventh weeks postpartum ($p < 0.05/4 = 0.0125$). Correlation analyses of the individual assessment sessions revealed that WB 5-HT concentrations correlated significantly with tension/anxiety scores in the third trimester ($r = –0.50$, $p < 0.0089$) and the third–fourth week postpartum ($r = –0.63$, $p < 0.0011$).

3.5. *Serum estradiol concentrations*

Mean serum estradiol concentration in the third trimester was 28053.6 ± 8757.6 pg/mL. It markedly decreased from the third trimester to the first (64.4 ± 54.6 pg/mL), third–fourth (14.24 ± 7.1 pg/mL) and sixth–seventh weeks postpartum (16.6 ± 9.6 pg/mL). Serum estradiol concentrations were within the clinically normal range at all time points assessed in this study.

3.6. *Plasma oxytocin concentrations*

The mean plasma OXT concentration obtained from 12 women 5–30 min after breastfeeding for 10–20 min in the first week postpartum was 31.5 ± 23.2 μU/mL, which was higher than the clinically normal range of non-pregnant women (< 5 μU/mL).

4. Discussion

This study is the first to show that mean WB 5-HT concentrations in postpartum lactating women are significantly higher in the late postpartum period (third–fourth and sixth–seventh weeks postpartum) than in the third trimester. Corresponding with this change in mean WB 5-HT concentrations, late postpartum mean tension/anxiety scores were significantly lower than those in the third trimester.

We found significant negative correlations between WB 5-HT concentrations and tension/anxiety scores in the third–fourth week postpartum and the third trimester. It is thus reasonable to hypothesize that the 5-HT system in the brain plays an important role in the regulation of tension/anxiety in pregnant/postpartum women. This hypothesis is in agreement with the anxiolytic effects of SSRIs, which increase synaptic 5-HT in the brain and facilitate 5-HT transmission by inhibited activity of 5-HT transporters. In fact, SSRIs are commonly used for treatment of postpartum depression (Appleby et al., 1997; Misri et al., 2004). There were no significant differences in mean WB 5-HT concentrations or mean tension/anxiety scores in the first week postpartum compared with either the third trimester or non-pregnant women.

It is well established that estradiol affects the activity of the 5-HT system by

inhibiting MAO-A (Smith et al., 2004), which is known to promote 5-HT degradation (Bethea et al., 2002). A recent positron emission tomography study (Sacher et al., 2010) has shown increased levels of MAO-A in various brain regions in women who were 4–6 days postpartum. Furthermore, the present study showed a marked decrease in estradiol after delivery. It is thus possible that the decreased estradiol concentrations after delivery cause disinhibition or activation of MAO-A, which would increase 5-HT degradation, resulting in inhibition of 5-HT system in the brain after delivery. We therefore propose that the 5-HT system in the brain is inhibited after delivery.

However, we found no significant differences in mean WB 5-HT concentrations or mean tension/anxiety scores in early postpartum compared with the third trimester. This result cannot be explained by the proposed inhibitory effect on the 5-HT system in the brain. This conflicting result may be explained by any excitatory effects on the 5-HT system in the brain which occur during the postpartum period. One possible excitatory factor would be the OXT release in the brain induced by infant suckling during the postpartum period, as described in detail later. Note that all postpartum women in this study breastfed their infants and continued to breastfeed throughout the evaluation period.

Using a microdialysis study during suckling in female rats, Neumann et al.

(1993) showed that lactation induces an increase in OXT in the brain. Furthermore, a recent review by Slattery and Neumann (2008) has indicated that increased brain OXT plays an important role in the hyporesponsiveness to stress (inhibitory effects on the hypothalamo-pituitary-adrenal axis) and reduction of anxiety.

OXT secreted in the maternal brain may excite 5-HT neurons in the brain and decrease anxiety. Yoshida et al. (2009) recently demonstrated that 5-HT neurons in the dorsal raphe nuclei in mice express OXT receptors. They also showed that OXT infusion into the raphe nuclei facilitates 5-HT release in the brain and reduces anxiety-related behavior. It is thus likely that OXT in the brain is one of the excitatory factors influencing 5-HT system in the brain during the postpartum period. The lack of change in mean WB 5-HT concentration and mean tension/anxiety score in early postpartum found in the present study may be explained by a combination of these excitatory and inhibitory mechanisms operating on the 5-HT system in the brain during the early postpartum period.

In the late postpartum period we found a significant increase in mean WB 5-HT concentrations accompanied by a significant decrease in mean tension/anxiety score. These results are compatible with the clinical observations that postpartum blues occur in the first week postpartum and most women with

postpartum blues recover quickly without treatment (Kennerley and Gath, 1986).

Because the estradiol level remained low in the late postpartum period, we hypothesize that the excitatory mechanism operating on the 5-HT system may be stimulated in the late postpartum. This hypothesis is supported by results from the clinical study by Johnston and Amico (1986), who prospectively studied the OXT release in response to infant suckling in healthy postpartum lactating women. Suckling-induced OXT release gradually increased throughout the first 6 months postpartum. OXT release was significantly increased in 5−14 weeks postpartum and peaked in 15−24 weeks postpartum compared with in 2−4 weeks postpartum. They concluded that the maximum OXT release is dependent on continuous regular nipple stimulation. Taking this into consideration, we hypothesize that the significant increase in mean WB 5-HT concentrations in the late postpartum period observed in this study is caused by a gradual increase in the lactation-induced OXT release during the postpartum period.

Although the hypothesis of OXT-induced excitation of the 5-HT system in the brain during the postpartum period seems to explain the present conflicting results, only a small portion of postpartum breastfeeding women participated in this experiment. This hypothesis should therefore be evaluated in future experiments.

Finally, we should validate our findings obtained by estimating the 5-HT levels in the brain from our measured WB 5-HT concentrations. An *in vitro* morphological study by Brust et al. (2000) and an *in vivo* physiological study by Nakatani et al. (2008) demonstrated that 5-HT transporters located on brain endothelial cells act as the efflux transport system for 5-HT that crosses from the brain into the circulating blood. Therefore 5-HT in the brain no doubt causes a change in 5-HT in the circulating blood. However, it is thought by some that increased 5-HT concentrations in the brain may not cause any significant changes in the 5-HT levels in the blood because it has been reported that > 90% of the total 5-HT content in the whole body is distributed within the gastrointestinal tract (West, 1958), and only a very small percentage of the total whole-body 5-HT content is found within the brain. Nakatani et al. (2008) showed in an *in vivo* functional study using rats undergoing gastrointestinal resection that WB 5-HT concentrations significantly increased whenever brain 5-HT levels were elevated. Therefore, increased 5-HT in the brain does contribute to a significant change in WB 5-HT concentration.

Furthermore, the well-established animal study by Jacobs and Fornal (1993) demonstrated that the activity of 5-HT neurons in the brainstem is enhanced by voluntary rhythmic behaviors including locomotion, mastication and breathing;

correspondingly, we previously reported increased WB 5-HT concentrations in humans after pedaling exercise (Fumoto et al., 2010), rhythmic mastication (Mohri et al., 2005) and Tanden breathing (Yu et al., 2011). Therefore, we are confident that increased 5-HT in the human brain can be estimated by a significant increase in WB 5-HT concentration.

The women continued to breastfeed their infants every 3 to 5 h throughout the evaluation periods, and thus the repetitive lactation-induced OXT release in the brain would activate the 5-HT system in the brain, resulting in elevation of maternal brain 5-HT levels. It is thus reasonable to hypothesize that such an increase in 5-HT in the brain would cause the increase in WB 5-HT concentrations found in the postpartum lactating women in this study.

In summary, the present study is the first to report increased blood 5-HT concentrations accompanied by reduced tension/anxiety during the late postpartum period in healthy lactating women. These results may be explained by a combination of inhibitory and excitatory mechanisms operating on the 5-HT system in the brain, namely rapid onset of inhibition induced by a marked decrease in estradiol after delivery and a gradual increase in excitation caused by brain OXT release, which is induced by infant suckling during the postpartum period.

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Figure Captions

Figure 1

Mean whole blood serotonin (WB 5-HT) concentrations in the postpartum group (n = 28) at the times indicated. Data are expressed as the mean ± SD. The horizontal broken line indicates the mean WB 5-HT concentration in the non-pregnant control group and the gray box indicates the SD in this group (159.2 ± 51.8 ng/mL, n = 28). **, $p < 0.01$; ****, $p < 0.0001$; within-subject effects in the postpartum group. ##, $p < 0.01$; as compared to the non-pregnant control group. 1W, first week postpartum; 3–4W, third–fourth week postpartum; 6–7W, sixth–seventh week postpartum.

Figure 2

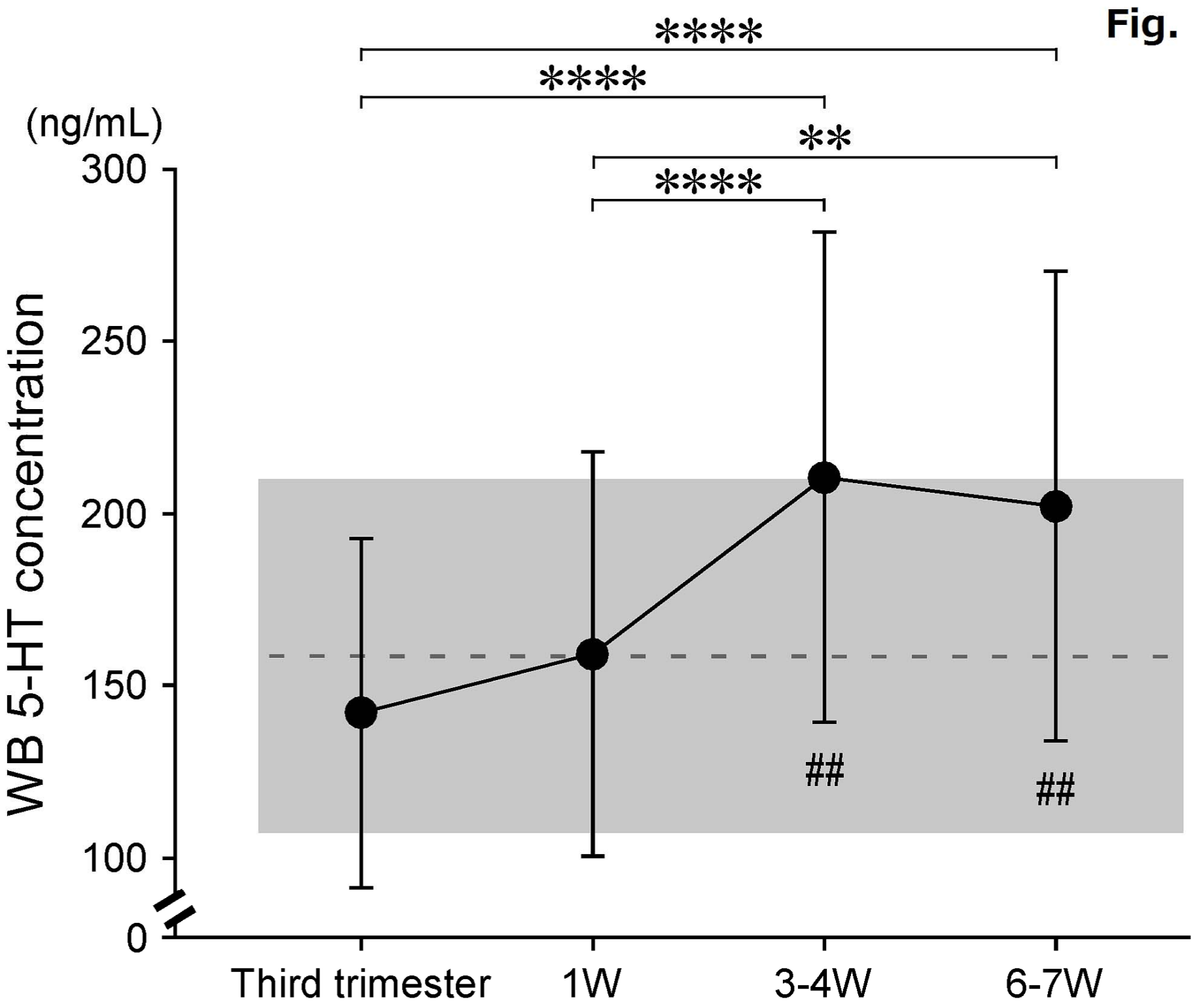
Mean scores for the Profile of Mood States subscales of (A) tension/anxiety, (B) vigor and (C) fatigue in the postpartum group (n = 28) at the times indicated. Data are expressed as the mean ± SD. The horizontal broken lines show the mean scores for the non-pregnant control group (n = 28), the SD being represented by gray boxes. *, $p < 0.05$; **, $p < 0.01$; within-subject effects in the postpartum group. ##, $p < 0.01$; compared with scores in the non-pregnant control group. 1W, first week postpartum; 3–4W, third–fourth week postpartum; 6–7W, sixth–seventh

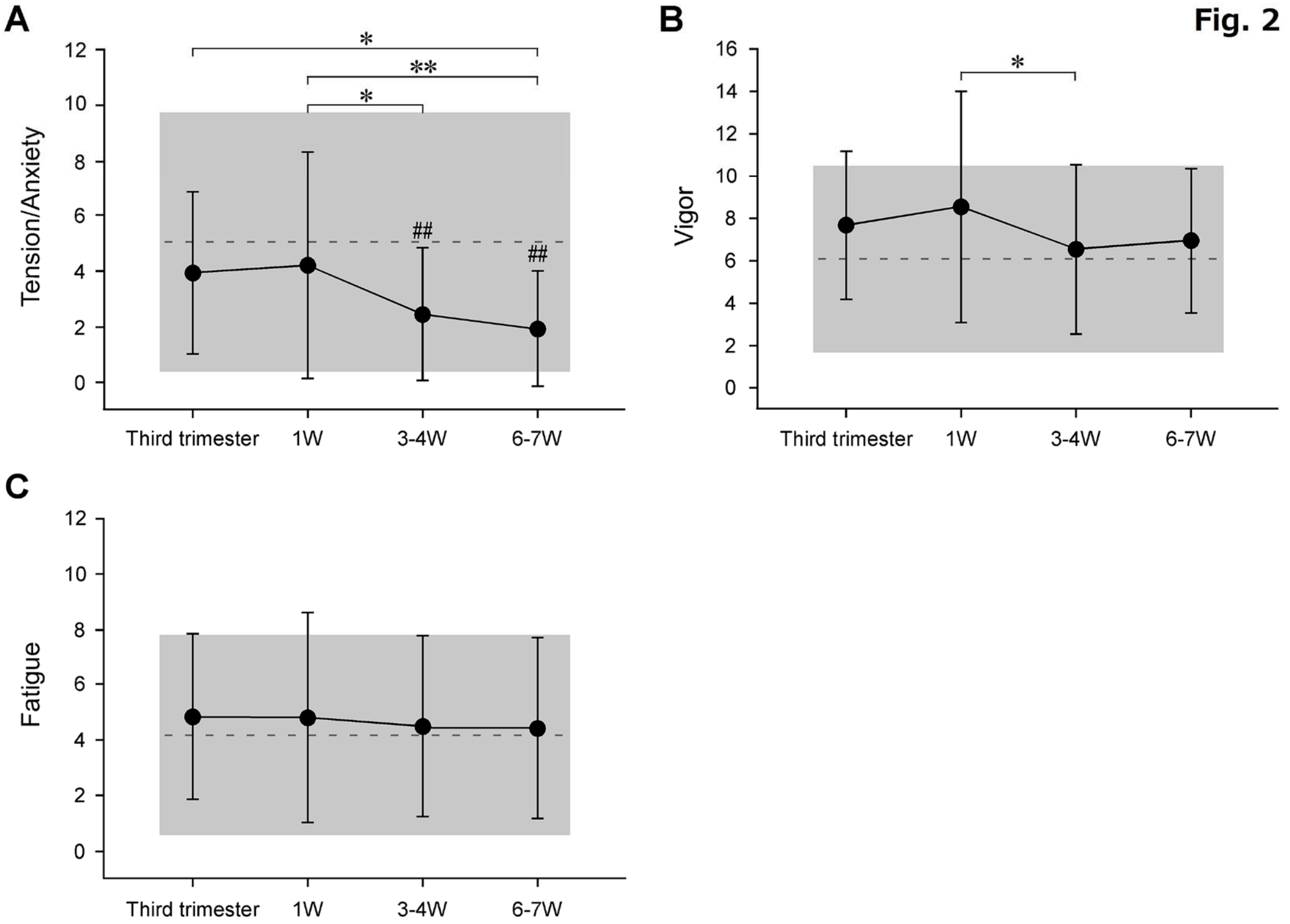
week postpartum.

Figure 3

Correlation between whole blood serotonin (WB 5-HT) concentrations and Profile of Mood States tension/anxiety scores of postpartum women at the times indicated ($n = 28$). Spearman's ranked correlation with Bonferroni correction was used ($p < 0.05/4 = 0.0125$). Significant correlations were found in the third trimester ($r = –0.50$, $p < 0.0089$) and third–fourth weeks postpartum ($r = –0.63$, $p < 0.0011$). 1W, first week postpartum; 3–4W, third–fourth week postpartum; 6–7W, sixth–seventh week postpartum.

Fig. 1


****
****
**
****
(ng/mL)
300
250
200
150
100
0
WB 5-HT concentration
##
##
Third trimester
1W
3-4W
6-7W


A
B
C
Fig. 2
Tension/Anxiety
Vigor
Fatigue
Third trimester
1W
3-4W
6-7W
*
**
##

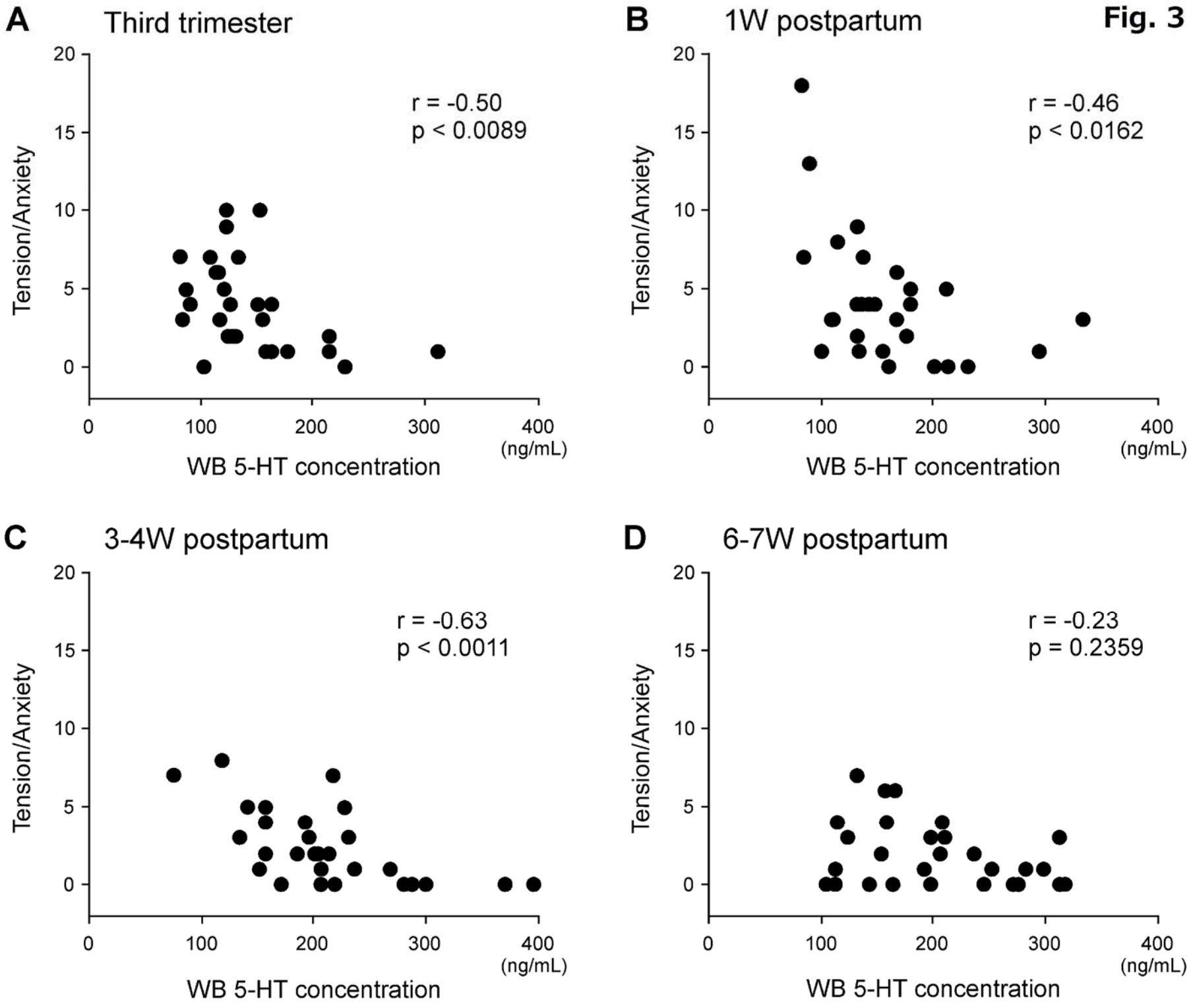

A
Third trimester
r = -0.50
p < 0.0089
B
1W postpartum
r = -0.46
p < 0.0162
C
3-4W postpartum
r = -0.63
p < 0.0011
D
6-7W postpartum
r = -0.23
p = 0.2359
Tension/Anxiety
WB 5-HT concentration
(ng/mL)
0
5
10
15
20
100
200
300
400

Fig. 3