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Original Article

Increased resting-state activity in the cerebellum with mothers having less adaptive sensory processing and trait anxiety

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Abstract

Child-rearing mothers with high levels of trait anxiety have a tendency for less adaptive sensory processing, which causes parenting stress. However, the neural mechanisms underlying this sensory processing and trait anxiety remain unclear. We aimed to determine the whole-brain spontaneous neural activity and sensory processing characteristics in mothers with varying parenting stress levels. Using resting-state functional magnetic resonance imaging, we assessed mothers caring for more than one preschool aged (2–5 years) child and presenting with varying levels of sensory processing, trait anxiety, and parenting stress. Spontaneous neural activities in select brain regions were evaluated by whole-brain correlation analyses based on the fractional amplitude of low-frequency fluctuations (fALFF). We found significant positive correlations between levels of sensory processing with trait anxiety and parenting stress. Mothers having less adaptive sensory processing had significantly increased resting-state network activities in the left lobule VI of the cerebellum. Increased fALFF values in the left lobule VI confirmed the mediation effect on the relationship between trait anxiety and sensory processing. A tendency for less adaptive sensory processing involving increased brain activity in lobule VI could be an indicator of maternal trait anxiety and the risk of parenting stress.

Keywords: amplitude of low-frequency fluctuations, cerebellum, parenting stress, resting-state fMRI, less adaptive sensory processing, trait anxiety

1 Introduction

Everyday life is full of various sensory stimuli. Sensory processing refers to the ability to regulate and organize reactions to sensory stimuli in a graded and adaptive manner (1-3). In other words, sensory processing refers to the ability of the brain to correctly respond to the surrounding environmental stimuli and remain at the correct responsiveness level. Sensory processing has been explained based on neurological threshold and behavioral response; the neurological thresholds refer to the intensity of stimuli needed for the central nervous system (CNS) to notice or react to stimuli, while the behavioral responses refer to the manner of response in relation to the thresholds (2).

Although most people present with balanced sensory processing abilities, approximately 15% of the population present with a tendency for less adaptive sensory processing patterns (4). The brains of individuals with a tendency for less adaptive sensory processing, who present hyper-responsive or hypo-responsive behaviors, are thought to be unable to receive stimuli or filter out irrelevant stimuli (5, 6); for example, "they startle easily from unexpected or loud noises," "they don't notice when other people come in the room," "they don't seem to notice when their hands or faces are dirty," "they are unaware of odors that others notice," " they keep the shades down," "they touch others when they're talking" (2, 4). The response process is not as automatic as that in most individuals and requires more effort for those with less adaptive tendency for sensory processing. This may interfere with engagement in daily activities such as eating, grooming, and socializing (6).

Healthy individuals with a tendency for less adaptive sensory processing, such as those with low sensory input registration or sensory hypersensitivity, have been shown to have high trait anxiety (7, 8). Trait anxiety predisposes individuals to daily evasive behavior as well as excessive and volatile emotions (9, 10). In adults with autistic traits, abnormal sensory processing is positively associated with trait anxiety (8). Sensory processing ability has been studied in adults with mental health issues (11, 12), including anxiety and social-emotional issues, and can predict psychological distress (13). Particularly, there is a strong association between trait anxiety and sensory processing difficulties, which can cause stress in routine situations.

Significantly, anxiety in child-rearing mothers is associated with depressive symptoms and care stress (14, 15). Increased trait anxiety in mothers has been shown to induce parenting stress (16). Moreover, a high level of trait anxiety in mothers is a risk factor for child maltreatment (17). A study of mother–child mutual play reported that mothers with increased trait anxiety were less sensitive to their child's behaviors (18). In addition, maternal anxiety is associated with less adaptive sensory processing even in healthy adults (19). Mothers with a tendency for less adaptive sensory processing were reluctant to respond promptly to their children's signs, including crying (20). Low threshold prenatal sensory patterns correlated with maternal–infant postnatal attachment (21).

In a study of the rearing brain, a mother's brain becomes sensitive to baby stimuli during the first months of life (22). In other words, child-rearing mothers are constantly exposed to the stimulus of their baby, in addition to other daily sensory stimuli. Mothers have a response bias to infant's facial stimuli, which is generally perceived as adaptive (23). As environment stimuli are also typically present, a process is envisioned in which unrelated stimuli are suppressed, and the target infant's facial stimulus unconsciously and consciously pops up. If there is a tendency for less adaptive sensory processing, such processing cannot be performed. In this case, the infant's facial expression input may be complex for the mother, leading to child-rearing stress. Taken together, these previous findings suggest that trait anxiety in mothers can influence a tendency for less adaptive sensory processing, which can lead to difficulties in parenting.

Trait and state anxiety are two psychological concepts essential to understanding how individuals respond emotionally and cognitively in different situations (24, 25). Trait anxiety is a stable and lasting tendency that defines a person's overall anxiety level across time and situations and is defined more as a personality feature (10). It is often seen as a fundamental part of someone's personality. People with high trait anxiety consistently feel uneasy, worried, and on edge in various circumstances, even without immediate stressors. This enduring trait can impact how individuals perceive threats, cope, and navigate their environment. The State-Trait Anxiety Inventory (STAI) assesses trait anxiety, helping to measure this relatively constant disposition.

In contrast, state anxiety is a temporary emotional state marked by a temporary increase in feelings of apprehension, tension, and nervousness, which is a temporary reaction to adverse events

(10). It arises in response to specific situations or stressors an individual encounters. Unlike trait anxiety, state anxiety varies depending on the perceived threat or challenge in the immediate context. This anxiety type is often linked to the 'fight or flight' response and is a natural adaptive reaction to perceived dangers. State anxiety is typically evaluated through self-report measures like the State portion of the State-Trait Anxiety Inventory (STAI-State), which captures a person's current emotional experience.

Thus, trait anxiety reflects a stable individual trait related to experiencing anxiety, while state anxiety captures the fluctuating emotional response to particular situations. A recent fMRI study has shown differences in resting-state functional connectivity (rs-FC) for healthy human trait anxiety and state anxiety. Furthermore, concerning structural gray matter (GM), trait anxiety was related to volume alterations in anterior cingulate, limbic regions such as the amygdala with and cingulate gyrus, precuneus, cuneus, and inferior frontal gyrus, and cerebellar involvement; the cerebellum was particularly strongly related (26). Additionally, previous studies show that sensory processing capacity (AASP) predicts psychological distress in adults with mental health problems (12, 27) and that lower sensory processing capacity is associated with higher trait anxiety (7, 8). Hence, the present study addressed only trait anxiety in parenting mothers to identify the neural basis of sensory processing with trait anxiety in a whole-brain search to show the relationship between trait anxiety, sensory processing capacity, and its neural basis.

Fractional amplitude of low-frequency fluctuations (fALFF) can reflect individual characteristics in healthy adults, including the "Big Five" personality traits (28), trait extroversion (29), trait empathy (30), trait grit (31), subjective well-being (32), trait hopefulness (33), and perceived stress (34). However, there are no studies on the characteristics of spontaneous neural activity in child-rearing mothers with a tendency for less adaptive sensory processing and trait anxiety using measurements of fALFF by resting-state functional MRI (rs-fMRI).

The tendency toward nonadaptive sensory processing induced by trait anxiety may be a stressor. Thus, it is unclear whether the effects of trait anxiety observed in mothers' parenting in everyday situations are mediated. Although neurobiology can elucidate the role of sensory processing in trait anxiety, relevant studies on the neural mechanism have been limited by their reliance on clinical samples with specific forms of psychopathology such as general anxiety disorder (35) and post-traumatic stress disorder (36).

Regarding the neural basis of sensory processing characteristics in healthy adults, studies have reported positive correlations of modality-specific (e.g., visual, auditory, or tactile) sensory scores with the gray matter volume in the related primary sensory areas (37). Moreover, the neural basis of sensory processing has been suggested to involve the neocortex, basal ganglia, and cerebellar activities (38). The neocortex is a sensory processor and elegant motor programmer. The basal ganglia and the cerebellum interact with the neocortex and have been involved in the adaptation and behavior of sensory information. In a recent study, connectome-based predictive modeling (CPM) suggested predicting maternal anxiety toward their infant between cerebellum and motor-sensory-auditory network and between frontoparietal and motor–sensory–auditory networks (39). Finally, the cerebellum has been suggested to be involved in emotion (e.g., anxiety) and motor control (36, 40). Accordingly, we hypothesized that the cerebellum is involved in trait anxiety, which involves less adaptive processing of sensory input in mothers.

Whole-brain exploration of fALFF analysis is suitable for exploring potential biomarkers through whole-brain investigation for the following reasons. First, fALFF assesses the amplitude of low-frequency oscillations across the entire brain, providing a comprehensive examination of regional neural activity and connectivity patterns. This approach allows researchers to investigate brain-wide alterations and identify potential biomarkers that might not be evident through region-specific analyses. Second, unlike region-of-interest (ROI) based analyses, whole-brain fALFF analysis does not rely on predefined brain regions or specific hypotheses (41). It allows for an unbiased exploration of the entire brain, enabling the identification of novel biomarkers and potential associations between brain alterations and clinical outcomes (42). Third, many neurofunctional disorders are characterized by widespread brain dysfunction rather than isolated abnormalities in specific regions. Whole-brain fALFF analysis captures such distributed alterations, which may be crucial in identifying reliable biomarkers with diagnostic or prognostic significance. In addition, some neurological or functional conditions might involve subtle changes in brain activity that are not readily apparent in conventional ROI-based studies. Whole-brain fALFF analysis can detect such subtle alterations, contributing to a deeper understanding of complex brain disorders (43). Lastly, the data-driven nature of whole-brain fALFF analysis allows for exploratory investigations without a priori assumptions. It enables researchers to discover unexpected associations and patterns, leading to new hypotheses and avenues for future research. Thus, whole-brain fALFF analysis is valuable for exploring potential biomarkers for neurological and functional disorders. Its unbiased and comprehensive nature makes it well-suited for identifying brain-wide alterations and their associations with clinical or subclinical phenotypes.

No previous brain MR imaging study has used rs-fMRI and sensory characteristics as a clue in studying women, especially mothers raising children. We here aimed to identify the neural correlates of sensory processing and trait anxiety using rs-fMRI exploratory fALFF analysis through a whole-brain search instead of the standard network analysis (ROI-ROI correlation analysis) to explore a potential biomarker. We also aimed to enroll child-rearing mothers for testing our hypothesis that subclinical anxiety reflects the atypical neural activity of brain regions involved in regulating sensory perception, sensory processing, and emotional behavior. Furthermore, we determined whether there was a correlation of alterations in regional brain activities with parenting stress.

2 Methods

2.1 Participants

Between 2015 and 2016, we enrolled 33 mothers (age range = 27–46 years, mean age = 35.9 years, standard deviation [SD] = 4.5 years) through advertisements targeted to female caregivers caring for more than one preschool, typically developing child, as previously described (44). The ethnicity of all participants was Japanese.

The study protocol was approved by the Ethics Committee of the University of Fukui, Japan (Approval # FU-20150109), and all procedures were conducted in accordance with the Declaration of Helsinki and the Ethical Guidelines for Clinical Studies of the Ministry of Health, Labor, and Welfare of Japan. The participants received explanations regarding the purpose and meaning of the study, and written informed consent was obtained from all subjects.

All participants had completed ≥12 years of education and were living above the relative poverty line, which is set at 50% of the median household income in Japan (Organization for Economic

Cooperation and Development, 2016). Based on self-report questionnaires, none of the participants had a history of brain injury, neurological or major psychiatric illness, current medication use, excessive alcohol intake, or cigarette smoking. Moreover, none of the participants were pregnant or had been diagnosed with or treated for depression or anxiety disorder. According to the Japanese version of the Flinders Handedness Survey (FLANDERS)(45), all the participants were classified as either right or left-handed.

All the participants met the safety requirements for undergoing rs-fMRI (exclusion of ferromagnetic implants, claustrophobia, pregnancy, and other factors). The standardized questionnaire was collected by mail after the brain imaging.

2.2 Psychological Questionnaires

Anxiety. We used the trait subscale of the State-Trait Anxiety Inventory (STAI), a 20-item self-reported questionnaire (10), to measure the participants' current anxiety mood. The STAI-Trait assesses how respondents "generally feel" (e.g., "I am a steady person" or "I lack self-confidence"). Each STAI-Trait item has a weighted score of 1–4. A rating of 4 indicates the presence of a high trait anxiety level.

Depression. The Beck Depression Inventory-II (BDI-II) (46) was used to measure the participants' current depressed mood. The BDI-II scores range from 0 to 63 with the cut-off points 14, 20, and 29 indicating mild, moderate, and severe depression levels, respectively.

Sensory processing. The Adult/Adolescent Sensory Profile (AASP) (47) was used to measure the participants' sensory processing degree. The AASP is a 60-item questionnaire designed as a trait measure of six sensory modalities involved in everyday sensory stimuli: visual (e.g., prefers darkness), auditory (e.g., holds hands over ears to protect them from sound), touch, taste/smell, movement (vestibular/proprioceptive), and activity level. It assesses how often the respondent performs a particular behavior using a 5-point scale (1, almost never; 2, seldom; 3, occasionally; 4, frequently; and 5, almost always; range of possible scores, 60–300). In contrast, the 60-item questionnaire is classified into four quadrants based on the Dunn's model (5). The four quadrants are defined by a "neurological threshold continuum axis" (i.e., behaviors hyper-responsive versus hypo-responsive to sensory stimuli) and a "passive-active behavior axis" (i.e., the person does/does not try to compensate behaviorally for an abnormal threshold). The AASP is the most widely used sensory processing scale in the world (48).

In a recent study, sensory processing problems were suggested to include sensory over-responsivity (SOR), under-responsivity (SUR), and seeking symptoms (1, 3). The SOR score used the sum of the avoidance quadrant and the sensitivity quadrant of the sensory profile score (1). Similarly, some or all four-quadrant scores are sometimes summed up (8, 49-52). The short sensory profile (SSP) version for children initially has a total score, and the higher the total score, the more atypical sensory processing (49, 53). However, in previous studies, the four-quadrant scores were often analyzed individually (7, 54).

Thus, the four quadrants of Dunn's model may overlap within an individual, as described in "At least one sensory quadrant of four quadrants" (55, 56). Initially, the four-quadrant scores of Dunn's model are closely related theoretically and statistically (7, 54). In particular, the "neurological threshold axis," which constitutes the four quadrants, has been confirmed to be continuous by skin conductance measurements and Electroencephalography (EEG), but the other "passive-active axis" has not been confirmed (4, 52). Therefore, we adopted the AASP total scores to confirm the neurological characteristics underlying individual differences in sensory processing (57).

Parenting stress. We used the Japanese version of the Parental Stress Index (PSI-J) (58) adapting the PSI (59) for measuring maternal parenting stress. The PSI-J is a 78-item self-report questionnaire, which is divided into child and parent rating items on a five-point scale that ranges from 1 (completely disagree) to 5 (completely agree). The child domain of stressors includes the child's adaptability and behavioral characteristics (e.g., degree to please parents, child's mood, degree to annoy parents, distractibility, and hyperactivity). The parent domain of stressors includes parental characteristics and feelings of social childcare support in the family (e.g., parental role restriction, social isolation, relationship with spouse, parental competence, depression/guilt, attachment, health). Higher scores indicate higher levels of parenting stress.

2.3 fMRI data acquisition

Scanning took place on the GE Discovery MR 750 3.0 Tesla scanner (General Electric, Milwaukee, WI, USA) using a 32-channel head coil. Functional images were acquired using a T2*-weighted gradient-echo echo-planar imaging sequence to produce 40 continuous transaxial slices with a thickness of 3.5 mm and 0.5 mm gap, respectively, covering the entire cerebrum and cerebellum (repetition time [TR] = 2300 ms; echo time [TE] = 30 ms; flip angle [FA] = 81°; field of view [FOV] = 192 mm; 64 × 64 matrix; voxel dimension = 3.0 × 3.0 mm; 201 acquisitions). During the scan, the participants were instructed to close their eyes, remain awake, and think of nothing in particular. We acquired high-resolution structural whole-brain images using a 3D T1-weighted fast spoiled-gradient recalled imaging sequence (TR = 6.38 ms; TE = 1.99 ms; FA = 11°; FOV = 256 mm; 256 × 256 matrix; 172 slices; voxel dimension = 1.0 × 1.0 × 1.0 mm).

2.4 fMRI data analysis

Preprocessing. To account for the time required for MRI signal equilibration and subject adaptation to the scanning environment, the first 10 volumes were discarded. The remaining 191 images were corrected for slice timing, followed by spatial realignment to correct for head motion. We adjusted for head motion effects by computing the mean frame-wise displacement (FD) (60). All participants' data were within the motion thresholds for inclusion in the analysis, defined as translational parameters <3 mm, rotational parameters <3°, and FD < 0.5. Subsequently, high-resolution T1 images were co-registered with the functional images using a nonlinear image registration approach. Next, images were segmented using a recently published diffeomorphic anatomical registration algorithm that employs an exponentiated Lie algebra technique (61). Subsequently, functional images were spatially normalized to the Montreal Neurological Institute template, resampled to a spatial resolution of 3 × 3 × 3 mm^3, and spatially smoothed with a 6-mm full width at half-maximum Gaussian kernel. Next, nuisance signals in 24 head-motion parameters (62), the global signal, the time series of the cerebrospinal fluid and white matter, and any linear trends were regressed out of each voxel's time course. Finally, we performed temporal band-pass filtering (0.01–0.8 Hz) of the residual time series to reduce the effect of low- and high-frequency drifts and noise, respectively (63).

Fractional amplitude of low-frequency fluctuations analysis. To investigate the spontaneous neural activity, we calculated the fALFF rather than the original ALFF because the former is considered less sensitive to physiological noise and artifacts that could weaken low-frequency oscillation approaches (60). To perform the fALFF calculation, the time course of each voxel signal was transformed into the corresponding power spectrum by fast Fourier transform (FFT). Subsequently, the power spectrum obtained by FFT was square-root-transformed and averaged across 0.01–0.08 Hz at each voxel, according to a previous study (64). The obtained averaged square root was divided by the global mean value, providing fALFF maps (65). Finally, for standardization, individual fALFF maps were divided by the grand average of the fALFF value. In order to perform a path analysis, we calculated the average value for each voxel in the cluster as a representative fALFF value for each subject.

Imaging data were preprocessed and analyzed using the Statistical Parametric Mapping software (SPM12; Wellcome Trust Centre for Neuroimaging, London, UK) and the Data Processing Assistant for rs-fMRI (DPARSF) (66) running on MATLAB R2016 (MathWorks, Natick, MA).

2.5 Statistical analysis

Statistical analyses were performed using SPSS Version 24 (IBM Corp., Armonk, NY). Data were expressed as mean ± SD. Using the datasets mentioned above, we performed a correlation analysis to investigate the relationships among trait anxiety, sensory processing characteristics, and parenting stress. Next, we performed a whole-brain correlation analysis of STAI and AASP total scores with fALFF values to determine the relationship between the degree of sensory processing and resting-state brain activities. The model included age, BDI-II scores, and mean FD as nuisance covariates. In addition, the mean FD, which was derived from individual analysis, was included to further exclude residual head-motion effects. The statistical threshold was set at $P < 0.005$ uncorrected at the peak level and $P < 0.05$ at the cluster level, with family-wise error (FWE) corrected over the whole brain. Further, we analyzed the correlation of the fALFF values with the STAI trait scores and the PSI total scores.

A path analysis mediated using the bootstrapping technique to obtain a 95% bias-corrected confidence interval (CI) of indirect effect was utilized to determine whether the fALFF value significantly mediated the association between trait anxiety and the degree of sensory processing. The bootstrap test was conducted using the R 3.1.2 Test package (http://www.R-project.org/).

3. Results

3.1 Descriptive statistics

Among the 33 participants, six were excluded (three did not fill out the questionnaire and three had a history of depression). Among the six excluded participants, one was not living above the relative poverty line and another was not married. All participants were unmedicated.

Artifact-free images suitable for rs-fMRI analyses were obtained from 27 female caregivers (age = 35.6 ± 4.3 years; AASP total scores = 141 ± 23.8; STAI trait scores = 42.6 ± 9.5; BDI-II scores = 11.3 ± 6.1; PSI total scores = 193.5 ± 40.7) who were caring for more than one preschool aged (2–5 years) child, including seven first-time mothers (**Table 1**). Of the 27 subjects, 25 were right-handed, and two were left-handed. None of the subjects exhibited severe anxiety, depression, abnormal sensory profiles, excessive parenting stress, or difficulties in child-rearing. The participants included four mothers with AASP total scores >1 SD (>164.8) from the mean.

Insert Table 1 here

There were significant positive correlations of sensory processing levels (AASP total scores) with the trait anxiety and with the PSI total (STAI, $r = 0.537$, $P = 0.004$; PSI, $r = 0.434$, $P = 0.024$, respectively) in mothers with various levels of sensory processing and parenting stress (**Figure 1A,**

B). There was no significant association between the AASP total scores and the BDI-II scores (*r* = 0.176, *P* = 0.381).

Questionnaire data are summarized in **Table 2**.

Insert Table 2 here

Insert Figure 1 (A), (B) here

3.2 Imaging results

We observed that individuals with higher AASP total scores had increased resting-state network activities in the left cerebellum, the region including lobule VI (Talairach's coordinates *x* = -30, *y* = -60, *z* = -24; cluster size = 80 voxels) (*P* = 0.008, FWE-corrected cluster level), as shown in **Figure 2.**

Insert Figure 2 here

None of the other values, such as the STAI trait and the PSI total scores showed a corrected cluster probability approaching significance. Without multiple comparison corrections, however, we found the result as an activity ($P < .005$, uncorrected at peak level, and $P < 0.05$, uncorrected at cluster level). Examination of voxels with decreased fALFF revealed no clusters anywhere in the brain. In lobule VI, fALFF values were significantly associated with the STAI scores (*r* = 0.466, *P* = 0.014). However, we observed no significant associations between the lobule-VI fALFF values and the PSI total scores (*r* = 0.306, *P* = 0.120).

We conducted a mediation analysis to assess the mediation effect of fALFF values in the left lobule VI. **Figure 3** shows the mediation model used for predicting AASP total scores. In this model, trait anxiety levels, left lobule VI fALFF, and AASP total scores were included as the independent variable, mediator, and dependent variable, respectively. Trait anxiety levels significantly predicted AASP total scores as indicated by previous multilevel regression analyses ($\beta = 0.537$, $P < 0.01$).

Further, trait anxiety levels predicted fALFF values in the left lobule VI (β = 0.466, P < 0.05). When trait anxiety levels and fALFF values in the left lobule VI were entered into the prediction model of the AASP total scores, there was a reduced effect of trait anxiety levels (β = 0.232, P = 0.114) while fALFF values in the left lobule VI remained significant (β = 0.655, P < 0.01). A bootstrapping procedure tested the mediating effect of fALFF values in the left lobule VI using 5,000 resamples. This technique yielded a 95% bootstrap CI without zero [0.010 to 1.883], which suggested that fALFF values in the left lobule VI significantly mediated the effect of trait anxiety on AASP total scores. We also developed a reverse causality model in which AASP predicts trait anxiety via the left lobule VI and examined its mediating effects. The results showed no significant indirect effect of AASP on STAI via left lobule VI （95% bootstrap CI [-0.15 to 0.22]).

Insert Figure ３ here

4. Discussion

To our knowledge, no previous brain MR imaging study has used rs-fMRI and sensory characteristics as a clue in studying women, especially mothers raising children. Thus, we performed a whole-brain exploratory fALFF analysis instead of the standard network analysis (ROI-ROI correlation analysis) to explore a potential biomarker through a whole-brain search. Our findings revealed an association between the degree of sensory processing evaluated using the AASP total scores and the resting-state brain activity in the left lobule VI (**Figure 2**). Individuals with higher AASP total scores had higher levels of both trait anxiety and parenting stress, as assessed by STAI and PSI scores, respectively (**Figure 1**). Additionally, path analysis showed that fALFF values in the left cerebellar lobule VI mediated the effect of trait anxiety levels on AASP total scores (**Figure 3**). This study elucidates the neural mechanism of the involvement of this region in sensory processing in mothers.

Notably, we observed a strong association between fALFF values in the left lobule VI of the cerebellum and the degree of sensory processing as measured by the AASP total scores. The reason for the association of functional brain activity alterations in left lobule VI with a less adaptive sensory processing phenotype remains unclear. Nonetheless, our findings are consistent with previous rs-fMRI studies using independent component analysis, which reported a functional connection between this region (lobule VI) and a salience network (67, 68). The salience network is involved in the detection and integration of emotional and sensory stimuli and the coordination of switching between internal and external cognition of the default mode network (69). The sensory processing scores, based on the Dunn model, suggest the ability to monitor and adjust information such that the CNS may generate appropriate responses to specific stimuli (2). Our finding that sensory processing scores were associated with left lobe VI supports that the salience network, including left lobe VI, is the neural basis of sensory processing. A previous study that assessed continuous cognitive processes and resting network switching in adults suggested lobule VI involvement (70). Importantly, lobule VI is the only region in the cerebellum that has been identified as crucially involved in switching from non-motor to motor functions (71). Thus, the mechanism of the association of the left lobule VI with a tendency for less adaptive sensory processing, including hypersensitivity and/or low registration of sensory stimuli, could play an important role in triggering correct responses to environmental stimuli.

Additionally, the lobule VI is associated with negative emotions such as fear, anger, and disgust (72). Individuals with higher sensory processing scores presented with higher trait anxiety scores (7, 8), and greater parenting stress (13, 16), which is consistent with the present report. A recent meta-analysis study on anxiety-related brain networks reported an association of high anxiety levels with attenuated connectivity within the salience and sensorimotor network (73). For example, adults with general anxiety disorder had low connectivity between the amygdala and the cerebellum. Therefore, our findings suggest that trait anxiety could induce less adaptive sensory processing at the subclinical level.

Although this finding has been discussed from the perspective of a potential cause-and-effect mechanism, our evidence only supports an association between sensory processing and the resting-state brain activity of lobule VI. The cerebellum is considered a general-purpose co-processor, with its effects being dependent on various brain centers connected to individual modules (67, 74) and a cerebellar timing process that contributes to sensory perception (75, 76). Conversely, participants with high lobule VI activation in the resting state could show subclinical but atypical levels of co-processor function, as well as atypical cerebellar timing processes in the sensory domain. Further, the cerebellum could be crucially involved in the pathogenesis of anxiety; cerebellar stimulation could potentially be used to treat psychiatric disorders by enhancing the cerebellar modulation of cognition and emotion (77, 78).

Notably, mediation analysis here revealed that trait anxiety symptoms in mothers affected the spontaneous neural activity of the left lobule VI. The tendency for less adaptive sensory processing in these individuals could be induced by subclinical trait anxiety levels, which may activate the resting-state network dynamics of the left lobule VI and prevent general-purpose processor function. Therefore, mothers who poorly register sensory input could present a continuous error signal to the cerebellum that does not habituate (79, 80). Subsequently, perception becomes disordered and the mother’s action toward the child seems illogical. Our findings are consistent with previous findings that mothers with high trait anxiety show poor responsiveness to the behavior of their child (18).

Specifically, we observed a correlation between the degree of sensory processing and both trait anxiety and levels of parenting stress. Moreover, the left-lobule-VI mediated between the degree of sensory processing and trait anxiety; however, cerebellar fALFF values were not correlated with parenting stress. Previous studies on parents have shown that human mothers adapt to parenting by means of reward-related motivational brain networks. In contrast, mothers with high levels of trait anxiety and invasive care tendencies employ different brain networks, including the stress-related occipital cortex and cerebellum (81, 82). Taken together, these findings suggest that was observed for less adaptive sensory processing, possibly induced by subclinical trait anxiety, could result in a compensatory increase in the resting-state brain activity of the cerebellum, which could be a risk indicator for parenting stress.

For mothers who have a tendency for less adaptive sensory processing, it is important to formulate an environmental setting and a support mechanism that is tailored to the situation of each individual mother in order to supplement sensory processing. In particular, mothers with increased fALFF values in cerebellar lobules VI who are more likely to respond to general daily sensory stimuli such as “hold your hand over your ear to protect your ear from sound,” and “I don't notice when people come in,” which makes it easy to feel parenting stress and anxiety. Clinicians may detect them early and intervene early, and provide specific advice of the form, "If you feel stressed about your baby's noisy crying, put your baby to sleep in a safe place, leave the place, and relax," "You may attach a bell on your child to make it easier to notice any movement," which will help reduce the stress and anxiety of rearing a child.

As shown in Table 2, the BDI-II scores strongly correlated with parenting stress. The relationship between parenting stress and depressive state has been extensively studied in psychological and parenting research (83, 84). Parenting stress and depressive state can influence each other in a bidirectional manner. High levels of parenting stress can contribute to developing or exacerbating depressive symptoms in parents. On the other hand, experiencing depressive symptoms can reduce a parent's ability to cope with parenting challenges, leading to increased parenting stress. Various factors can contribute to parenting stress, including the child's behavior, developmental challenges, financial pressures, lack of social support, and the parent's coping abilities. Thus, parenting stress and depressive state are closely related and can have significant implications for both parents' mental well-being and the parent-child relationship. Recognizing and addressing parenting stress through supportive interventions can be essential in preventing or alleviating depressive symptoms in parents and promoting overall family well-being (83). Adequate social support, coping skills, and self-care practices can act as protective factors against parenting stress and depressive symptoms. Enabling caregivers to seek help by engaging supporters in proactive coping strategies is essential to mitigate the adverse effects of parenting stress on mental health.

This study has several limitations. First, the study design and lack of a control group comprised of patients with anxiety disorders or neurodevelopmental disorders limit the validity of our findings. We could not enroll such a patient group because we aimed to employ rs-fMRI as an unbiased whole-brain approach for identifying the neural correlates of sensory processing and trait anxiety in child-rearing mothers without other severe psychopathology or at high risk for anxiety disorder. However, given the paucity of findings on this topic, we believe that our contribution is important. Second, the method of assessing sensory processing using a self-reported questionnaire runs the risk of missing problem screening that the caregiver is having. For example, they may not be aware of their hypersensitivity or insensitivity, or they may not recognize the questionnaire items accurately and respond appropriately. In addition, because all the psychometric assessments were self-reported, we ran the risk of including participants with sensory processing disorders. Conversely, professional evaluation of healthy individuals without sensory processing disorder is as difficult as evaluating participants with a specific diagnosis. Consequently, without self-reporting, there is a risk of confounding neuroimaging differences associated with sensory processing and trait anxiety with those involved in enhanced resilience. Taken together, the evidence indicates that the imaging differences observed in our participants can be generalized to the general population because they are outcome independent.

Third, this study was performed in a naturalistic setting with some participants having missing data, and consequently being excluded. Therefore, we cannot rule out the possibility of positive selection bias. Positive selection bias occurs when missing values are not randomly distributed in a dataset, but instead, specific values are more likely to be missing than others. In a naturalistic setting, this bias could occur if participants with specific characteristics or conditions are likelier to drop out or be unavailable for data collection (85). Also, positive selection bias can distort the results by introducing a non-random pattern of missing data, which may not represent the entire population under study. This bias can lead to overestimating or underestimating associations between variables. Thus, we should carefully analyze missing data patterns to mitigate positive selection bias and explore potential reasons for the missingness.

Fourth, this study had a cross-sectional design that precluded the identification of causal links between trait anxiety, sensory processing, and its impact on the brain functions of mothers beyond statistical causal inference based on cross-sectional data. Longitudinal studies are required to elucidate these associations fully. Fifth, although the present study was conducted with mothers raising children typically, future studies will need to consider more essential control groups, such as adult men and women not in the child-rearing years. Sixth, in the present study with multiple comparison corrections, no salience/default mode network-related regions other than the cerebellum may be due to sample size or sample characteristics such as childrearing mothers. Lastly, we used the

PSI scale in the present study. Additional studies are needed to measure brain activity further while a mother interacts with her child (i.e., mother and child play tasks analyzed through an MRI scanner) to evaluate the influence of sensory processing on mother–child interaction. Sixth, state anxiety was not measured in the present study. In order to further study the subject/mother's anxiety tendency and sensory processing from various perspectives, it may be necessary to examine state anxiety as well.

In summary, this study demonstrates evidence for a neurofunctional indicator underlying various levels of trait anxiety and less adaptive sensory processing by the fALFF values in the left cerebellar lobule VI in a sample of child-rearing mothers. Further, the discussed findings indicate that fALFF could be a clinically meaningful measure for detecting maternal trait anxiety as a factor for parenting stress. Determination of this measure for daily sensory stimulation could be used to screen for parents at risk of maltreating their child for delivery of early guidance interventions, and to further elucidate individual differences within various levels of trait anxiety and parenting stress. These results of our study are promising results for clinical application. The fALFF value offers several advantages over self-reported questionnaires like STAI and PSI-J. Such MRI assessment provides an objective and direct measurement of brain function, whereas self-reported questionnaires rely on subjective responses from individuals. MRI allows researchers to visualize and quantify brain regions and their activities directly, providing more concrete and accurate data. Thus, it can assess brain activity related to anxiety or stress, even when participants are unaware of these processes. On the other hand, self-reported questionnaires rely on participants' conscious awareness and may not capture unconscious or subtle emotional experiences.

Despite these advantages, it is essential to acknowledge that MRI assessments have some limitations, including cost, technical expertise requirements, and potential claustrophobia or discomfort for specific individuals during the scanning process. Therefore, combining MRI and self-reported questionnaires can provide a more comprehensive understanding of psychological and neurobiological factors.

One strength of this study is that it allows for future longitudinal and comparative rs-fMRI studies on different levels of sensory processing in mothers to assess parenting stress. To accumulate such research findings, it will be possible in the future to establish treatments (psychoeducations) tailored to individuals who have various sensory processing patterns, which will adequately mitigate parenting stress and anxiety. Taken together, we believe that these approaches, including early screening and psychoeducation, are critical for assisting mothers to cope with a tendency for less adaptive sensory processing during their parenting period and to form a stable attachment with their child, which could help prevent child maltreatment.

Author contributions: A. T. conceived the project. N.S., and A.T. designed the experiments. N.S., K.M., R.K., T.X.F., and A.T. performed the experiments, collected the data, and analyzed the data. N.S. R.K. and A.T. wrote the manuscript. All authors have read and approved the final manuscript.

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Institutional Review Board Statement: The study protocol was approved by the Ethics Committee of the University of Fukui, Japan (Approval # FU-20150109), and all procedures were conducted in accordance with the Declaration of Helsinki and the Ethical Guidelines for Clinical Studies of the Ministry of Health, Labor, and Welfare of Japan.

Informed Consent Statement: The participants received explanations regarding the purpose and meaning of the study, and written informed consent was obtained from all subjects.

Data availability statement: The data cannot be made publicly available as data sharing was not included in the consent form.

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Table 1. Participants' demographic characteristics and psychological questionnaires score (n = 27).

	Mean	**SD**	**Range**	**%**
Age (years)	35.6	4.3	27-43	
Right-handed				84.8
Completed at least 12 years of education				100
Married (non-divorced, non-widowed)				100
Number of family members	4.6	1.1	3-7	
Number of children	2	0.8	1-4	
Months since last childbirth	31	1.7	1-69	
Living above the relative poverty line				100
State-Trait Anxiety Inventory: Trait Score	42.6	9.5	25-63	
Beck Depression Inventory-II Score	11.3	6.1	2-23	
Adult/Adolescent Sensory Profile Score (total)	141	23.8	95-214	
Quadrant scores Low Registration	31.4	6.8	22-55	
Sensation Seeking	40.2	5.7	32-55	
Sensory Sensitivity	36.6	9.1	18-61	
Sensation Avoiding	32.9	8.8	20-53	
Modality-specific subscales Visual	24.6	4.8	17-33	
Auditory	24.6	6.3	15-43	
Touch	31.2	7.2	20-55	
Taste/smell	17.5	3.9	10-24	
Movement (vestibular/proprioceptive)	17.4	3.4	11-27	
Activity level	25.8	4.6	17-37	
Parenting Stress Index Score (total)	193.5	40.7	118-302	
Child Domain Score	86.3	18.7	51-122	
Parent Domain Score	107.3	25.6	64-180	

Table 2. The correlations between psychological questionnaires score

	Psychological Questionnaires	Correlation 1	2	3	4	5	6	7	8	9	10
1	**State-Trait Anxiety Inventory：Trait Score**										
2	**Beck Depression Inventory- Ⅱ Score**	.608**									
3	**Adult/Adolescent Sensory Profile score(total)**	.537**	.176								
4	Low Registration	.478*	.152	.760**							
5	Sensation Seeking	-.016	-.105	.512**	.394*						
6	Sensory Sensitivity	.563**	.223	.902**	.597**	.213					
7	Sensory Avoiding	.507**	.194	.844**	.406*	.207	.799**				
8	**Parenting Stress Index Score(total)**	.681**	.748**	.434*	.514**	.155	.316	.345			
9	Child Domain Score	.484*	.674**	.375	.351	.153	.257	.373	.888**		
10	Parent Domain Score	.729**	.698**	.416*	.560**	.135	.314	.276	.942**	.681**	

** $P < .01$, * $P < .05$

Figure Legend

Figure 1 (A) Scatterplot showing the relation between trait scores from the STAI and AASP total scores. (B) Scatterplots showing the relation between PSI scores and AASP total scores. STAI, State-Trait Anxiety Inventory; AASP, Adult/Adolescent Sensory Profile; PSI, Parenting Stress Index.

Figure 2 Brain regions with *significantly increased resting-state network activities*, measured as fractional amplitude of low-frequency fluctuations (fALFF) using a fast Fourier transform. The main cluster is in the left cerebellum, lobule VI; Talairach's coordinates $x = -30$, $y = -60$, $z = -24$; cluster size = 80 voxels; $Z = 4.06$, family-wise error-corrected cluster level. Color scale represents t-values in the range 0–5.

Figure 3 Path model of the mediation effect of resting-state activity (fALFF values) in the left cerebellum, lobule VI, on the relationship between degree of trait anxiety, measured as the trait scores of the State-Trait Anxiety Inventory (STAI), and sensory modulation (AASP total scores). fALFF, fractional amplitude of low-frequency fluctuations; AASP, Adult/Adolescent Sensory Profile, SE, standard error; β, Standardized partial regression coefficient; *, $P < .05$; **, $P < .01$; n.s., not significant.