Prenatal exposure to antidepressants and depressed maternal mood alter trajectory of infant speech perception

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Language acquisition reflects a complex interplay between biology and early experience. Psychotropic medication exposure has been shown to alter neural plasticity and shift sensitive periods in perceptual development. Notably, serotonin reuptake inhibitors (SRIs) are antidepressant agents increasingly prescribed to manage antenatal mood disorders, and depressed maternal mood per se during pregnancy impacts infant behavior, also raising concerns about long-term consequences following such developmental exposure. We studied whether infants’ language development is altered by prenatal exposure to SRIs and whether such effects differ from exposure to maternal mood disturbances. Infants from non–SRI-treated mothers with little or no depression (control), depressed but non–SRI-treated (depressed-only), and depressed and treated with an SRI (SRI-exposed) were studied at 36 wk gestation (while still in utero) on a consonant and vowel discrimination task and at 6 and 10 mo of age on a nonnative speech and visual language discrimination task. Whereas the control infants responded as expected (success at 6 mo and failure at 10 mo) the SRI-exposed infants failed to discriminate the language differences at either age and the depressed-only infants succeeded at 10 mo instead of 6 mo. Fetuses at 36 wk gestation in the control condition performed as expected, with a response on vowel but not consonant discrimination, whereas the SRI-exposed fetuses showed accelerated perceptual development by discriminating both vowels and consonants. Thus, prenatal depressed maternal mood and SRI exposure were found to shift developmental milestones bidirectionally on infant speech perception tasks.

infancy | maternal depression | critical periods

language, our most quintessential human characteristic, involves a complex interplay between biology and experience. At birth, infants possess an initial preparedness for language and a developmental readiness that supports learning any of the world’s languages (1–3), yet also already show privileged processing to the native language from prenatal listening experience (4–6). During the following weeks and months of life, infants become progressively attuned to the properties of their native language, including its rhythmical and segmental (e.g., consonant) information (reviewed in refs. 7 and 8). The high degree of regularity in the timing of sequential tuning to properties of the native language suggests a series of critical or sensitive periods, i.e., points in development when the system is maximally influenced by input. The timing of onset of these sensitive periods seems to be maturationally constrained. Infants born 3 mo preterm attune to the phonetic properties (9) of their native language at the same gestational age as full-term infants, not according to the number of months of postnatal listening experience. Such maturational constraints can protect development: ensuring the optimal consensive stabilization of the perceptual components that contribute in a step-wise fashion to language acquisition (10). However, it is known from research in other systems that highly aberrant input, and/or exposure to drugs or disease can change the timing of critical periods. For example, research with nonhuman animals shows that the timing of brain plasticity in the visual system can be shifted forward or reopened after closure by pharmacological manipulations, and that total sensory deprivation from birth (i.e., dark rearing) can delay the onset and closure of relevant critical periods (11). There are situations in which human infants are exposed to pharmacological agents and/or biological disparities that alter experience even in utero. Could such exposure shift the timing of sensitive periods in language development that typically appear to be maturationally controlled?

Prenatal exposure to maternal mood disturbances and antidepressants used to manage these disorders are exemplars of two increasingly common early life experiences that have long-term effects on behavior and development in childhood (12). During pregnancy, 15% to 20% of women experience mood disorders (e.g., depression) and between 5% and 13% of pregnant women are treated with an antidepressant drug (13, 14). Serotonin reuptake inhibitor (SRI) antidepressants are among the most commonly used drugs during pregnancy (14). Animal models have reported that perinatal antidepressant exposure impairs early 5-hydroxytryptamine (5-HT) homeostasis, influences mature cortical network function [e.g., development of the auditory (15) and somatosensory cortex (16)], and affects long-term neurobehavior (17, 18). Our understanding of similar neuroanatomical and functional consequences in humans is limited. Because SRIs readily cross the placenta and the blood–brain barrier (19), concerns have been raised about the developmental consequences of altered fetal 5-HT signaling (12, 20) or other downstream consequences (21) following prenatal SRI exposure. Importantly, antenatal maternal mood disturbances also have adverse consequences on later cognitive and language development (22–24) and affect early 5-HT levels (25), leading to confusion about how to distinguish the developmental impact of SRIs from antenatal maternal mood disturbances.

Given the neurobehavioral consequences of SRI exposure and depressed maternal mood, we asked whether exposure to SRIs or to gestational maternal depression (not treated with an SRI) has an impact on the timing and precision of speech perception milestones. To provide a sensitive assay in humans, we tested infants on two perceptual tasks that have been extensively studied: (i) auditory discrimination of a nonnative consonant speech sound...
contrast (26) and (ii) visual discrimination of the change from one language to another while watching silent talking faces (27).

For the auditory task, we tested discrimination of the Hindi phonetic contrast between dental /da/ vs. retroflex /Da/ alveolar stops, a distinction both English- and Hindi-learning infants have been shown to discriminate as young infants. Listening experience maintains discrimination of this distinction in Hindi-learning infants, but English-learning infants who do not hear this distinction regularly show a dramatic decline in discrimination performance by 10 mo of age (26, 28). Speech perception was tested by using a modified version of the alternating/nonalternating procedure (Materials and Methods). Infants were habituated to the dental /da/ sound and then played instances of the same /da/ sound (i.e., nonalternating trial) or a new trial with alternating dental /da/ and retroflex /Da/ sounds. Discrimination in this procedure is indicated by longer looks during the alternating test trials that include the new /Da/ sound.

The visual language discrimination task tested a similar age-related decline in perceptual discrimination. Young infants visually tell apart English and French at 4 and 6 mo of age, but fail at 8 mo unless they are raised bilingual (27, 29). As in the earlier work of Weikum et al. (ref. 27 and Materials and Methods), infants were habituated to silent video clips of three bilingual speakers reciting sentences in English and then immediately shown test trials of the same three speakers silently reciting sentences in French. Discrimination in this task is indicated by a recovery in looking time during the test trials.

We tested infants at 6 mo of age, before they typically experience a decline in sensitivity to nonnative language information, and again at 10 mo, by which time typically developing infants show a decline in performance on each task. We compared three groups of infants at each age: SRI-exposed infants whose depressed mothers had been prescribed SRI medications during pregnancy, depressed-only infants whose mothers had depressive symptoms but chose not to take medication, and control infants whose mothers did not meet our criteria for depression or take psychotropic medications during pregnancy. Maternal depression at the time of testing was included as a covariate.

We predicted that infants exposed to neither depressive maternal symptoms nor SRIs would show discrimination on both tasks at 6 mo, but fail at 10 mo as their sensitive period for nonnative language and auditory information begins to close. If SRI exposure and/or maternal mood impact the timing of sensitive period closure, the discrimination profile would be different. Acceleration would be shown by a failure to discriminate in the auditory and/or visual task already at 6 mo, whereas a delay in sensitive period closure could be shown by continued success even at 10 mo of age.

To complement our test of the timing of sensitive period closure, we also tested the participants at a time when their speech sound categories would be developing or “opening.” At 36 wk gestation, typically developing fetuses are capable of discriminating vowel sounds (e.g., /a/ and /i/) (30, 31), but no evidence exists for consonants. We tested 36 wk-gestation fetuses on discrimination of a consonant (/da/ as in “dot” vs. /ta/ as in “tot”) and a vowel (/a/ as in “ah” vs. /i/ as in “ee”) contrast. Fetal heart rate was recorded in response to stimuli presented via a speaker pointed at the mother’s abdomen. The sounds were modified and amplified to ensure transmission across the uterine wall (Materials and Methods). The previous work would predict success in the vowel but not the consonant condition. Developmental acceleration would be indicated by successful discrimination of both the vowel and consonant distinction, whereas disruption would be indicated by failure on both.

Results

Infant Age: 6 and 10 Mo. In the first experiment comparing performance at 6 and 10 mo, 32 control infants, 21 infants of non–SRI-treated prenatally depressed mothers, and 32 infants of SRI-treated depressed mothers were analyzed. Maternal and infant characteristics are listed for all participants (Table 1). There were no significant differences across groups in the mothers’ demographics, but mothers in the SRI-exposed and depressed-only groups reported significantly higher levels of depression [i.e., Hamilton Rating Scale for depression (HAM-D) scores] prenatally and at time of testing (Table 1). There were no significant differences in the number of trials required to reach habituation criterion, number of male and female sex, or birth characteristics across the three groups of infants.

Repeated-measures analyses of covariance (ANCOVAs) were used to compare trial (alternating vs. nonalternating for the auditory Hindi discrimination task, habituation vs. switch for the visual language task), and prenatal exposure group (control, depressed-only, or SRI-exposed). Concurrent postnatal maternal mood was controlled by adding the mother’s score on the HAM-D on the day of testing as a covariate. SRI exposure included all medications listed in Table 1 because our small sample sizes for each type of SRI did not permit further analysis of differential drug outcomes. Effect sizes ($\eta^2$) estimating the magnitude of the difference between the variables are reported.

Hindi sound discrimination at 6 mo. Controlling for maternal mood at 6 mo, a repeated-measures ANCOVA examining trial (alternating or nonalternating) and exposure group (control, depressed-only, SRI-exposed) revealed a significant within-subjects interaction for trial by exposure group ($F(2,67) = 4.376, P = 0.016, \eta^2 = 0.116$). When split according to exposure group at 6 mo, there was a significant main effect for trial in the control group: the infants looked signficantly longer during the alternating trials [$F(1,24) = 9.271, P = 0.006, \eta^2 = 0.279$]. A nonsignificant trend, but favoring the alternating or familiar trial, was found in the depressed-only group [$F(1,18) = 2.490, P = 0.12, \eta^2 = 0.122$]. There were no significant effects in the SRI-exposed group [$F(1,26) = 0.306, P = 0.585, \eta^2 = 0.012; Fig. 1A$].

Hindi sound discrimination at 10 mo. When split according to exposure group at 10 mo, there were no significant interactions or differences for infants in the control group [$F(1,27) = 0.058, P = 0.812, \eta^2 = 0.002$] or SRI-exposed groups [$F(1,29) = 0.144, P = 0.708, \eta^2 = 0.005$], but there was a significant main effect for trial in the depressed-only group [$F(1,15) = 5.886, P = 0.028, \eta^2 = 0.282; Fig. 1B$]. At this age (10 mo), infants in the depressed-only group looked longer during the alternating trials (similar to the 6-mo controls). An exploratory follow-up multivariate ANOVA of the depressed-only group at both ages revealed a significant interaction between 6 and 10 mo [$F(2,33) = 8.382, P = 0.007, \eta^2 = 0.203$], confirming the change from a familiarity (i.e., nonalternating) to a novelty (i.e., alternating) preference.

Visual language discrimination at 6 mo. Controlling for maternal mood at 6 mo, a repeated-measures ANCOVA examining trial (final habituation vs. test), and exposure group (control, depressed-only, SRI-exposed) revealed a significant within-subjects main effect for trial [$F(1,58) = 5.337, P = 0.024, \eta^2 = 0.084$] and trial-by-maternal mood interaction [$F(1,58) = 5.192, P = 0.026, \eta^2 = 0.082$]. There was also a significant between-subjects main effect for exposure group [$F(2,58) = 3.160, P = 0.05, \eta^2 = 0.098$]. Because there was a significant interaction for mood in the overall ANCOVA, the follow-up analyses at 6 mo split the data according to exposure group and controlled for maternal mood at 6 mo.

In the control group there was a significant difference between the final habituation and test trials [$F(1,24) = 13.954, P = 0.001, \eta^2 = 0.368$] and a significant interaction between trial and maternal mood at time of study [$F(1,24) = 7.434, P = 0.012, \eta^2 = 0.237$]. A follow-up linear regression analysis revealed a negative correlation between looking time to the switch and maternal depression [$B(1,24) = -0.486, P = 0.012, r^2 = 0.237$]. No significant differences were found for the depressed-only [$F(1,11) =$
0.09, $P = 0.926, \eta^2 = 0.001$] or SRI-exposed groups [$F(1,21) = 0.613, P = 0.442, \eta^2 = 0.028$; Fig. 2$^A$.]

**Visual language discrimination at 10 mo**. When split into exposure groups and analyzed at 10 mo (controlling for maternal mood at 10 mo), there were no significant differences for the control [$F(1,18) = 1.626, P = 0.218, \eta^2 = 0.083$] or SRI-exposed groups [$F(1,21) = 0.031, P = 0.861, \eta^2 = 0.001$], but the depressed-only group showed a significant main effect for trial [$F(1,14) = 6.023, P = 0.028, \eta^2 = 0.301$; Fig. 2$^B$]. Like the 6-m-old infants in the control group, the 10-m-old infants in the depressed-only group increased their looking to the language switch.

**Fetal consonant and vowel discrimination**. In the second experiment, 14 fetuses of mothers taking SRI medications during their pregnancy and 20 nonexposed fetuses were tested. With the exception of higher depressive symptoms in the SRI-treated group (based on HAM-D score), maternal demographic and health characteristics did not differ between the groups (Table 2). Independent-samples Mann–Whitney U comparisons were used to examine infant state (asleep/awake) at the time of the study and showed no significant difference between the state of the infants in the control group versus the SRI-exposed group for the consonant study ($P = 0.191$) or vowel study ($P = 0.503$).

As the sample size was not adequate for three groups, the effect of prenatal maternal mood was controlled by including it as a covariate. Heart rate deceleration during a 10-s window was used as the dependent variable following a switch in speech sound delivered from a speaker to the mother’s abdomen (*Materials and Methods*). It was predicted that nonexposed fetuses would discriminate the vowel contrast but not the consonant contrast.

The vowel discrimination data were analyzed by using two-by-two-by-10 [group (exposed vs. nonexposed) by trial type (preswitch vs. postswitch) by test trial] repeated-measures ANCOVAs, with maternal mood score (per HAM-D) at 36 wk gestation included as a covariate. There were no significant main effects, but there was a significant interaction between trial type (preswitch vs. postswitch) and test trial [$F(1,31) = 3.91, P = 0.051, \eta^2 = 0.11$] and a significant trial type-by-test trial-by-maternal mood (per HAM-D) interaction [$F(1,31) = 4.18, P = 0.025, \eta^2 = 0.12$].

To probe these significant interactions, a repeated-measures ANOVA using prenatal maternal mood (per HAM-D) as a

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**Table 1. Participant characteristics at 6 and 10 mo**

- **Characteristic** | **Control** | **Depressed only** | **SRI-exposed**
- **Maternal details** | | | |
- Prenatal HAM-D (56) | 3.61 ± 2.01 | 12.95 ± 4.93 | 10.67 ± 4.97 |
- 6 mo HAM-D (56) | 4.11 ± 3.99 | 11.42 ± 5.85 | 10.93 ± 6.58 |
- 10 mo HAM-D (56) | 3.57 ± 3.60 | 11.05 ± 7.58 | 10.07 ± 7.52 |
- Education (y) | 18.91 ± 3.65 | 17.71 ± 3.02 | 17.38 ± 3.84 |
- **Prenatal SRI medications (median mg/d)** | | | |
- Paroxetine | 0 | 0 | 0 |
- Fluoxetine | 0 | 0 | 0 |
- Sertraline | 0 | 0 | 0 |
- Citalopram | 0 | 0 | 0 |
- Escitalopram | 0 | 0 | 0 |
- Venlafaxine | 0 | 0 | 0 |
- Alcohol (no. of drinks during pregnancy) | 4.39 ± 8.60 | 4.67 ± 6.00 | 4.69 ± 8.45 |
- Smoking (yes/no) | 0 | 0.05 ± 0.22 | 0.03 ± 0.18 |
- Age at delivery (y) | 33.47 ± 3.88 | 36.3 ± 5.95 | 33.56 ± 5.90 |
- **Infant details** | | | |
- Sex (M/F) | 14/18 | 12/9 | 14/18 |
- Birth gestational age (wk) | 39.79 ± 1.45 | 39.78 ± 1.81 | 38.96 ± 1.48 |
- Birth weight (g) | 3448 ± 503 | 3530 ± 441 | 3267 ± 440 |
- Duration of prenatal SRI exposure (d) | | | |
- Age at 6 m study (d) | 183.96 ± 5.61 | 186 ± 6.15 | 184.57 ± 5.67 |
- Age at 10 m study (d) | 307.03 ± 7.16 | 308.89 ± 7.47 | 306.43 ± 4.33 |

*Significant at $P < 0.05$.}

**Fig. 1.** Comparison of alternating (Hindi dental and retroflex) trials to nonalternating (Hindi dental) trials after being habituated to Hindi dental syllable (*$P < 0.05$). Error bars represent SEM. (A) Data from control ($n = 25$), depressed-only ($n = 19$), and SRI-exposed infants at 6 mo ($n = 27$). (B) Data from control ($n = 28$), depressed-only ($n = 16$) and SRI-exposed ($n = 30$) infants at 10 mo.
There was a significant difference in the preswitch condition test trials and postswitch condition test trials. There was no significant difference in the preswitch condition, but a change in heart rate in the postswitch condition \( [F(1,31) = 3.08, P = 0.05, \eta^2 = 0.09] \). Pair-wise comparisons revealed a significant decline in heart rate between trials 2 and 4 \( (P < 0.05) \), with no main effect or interaction for exposure group or maternal mood (Fig. 3A).

The consonant data were analyzed by using the same two-by-two-by-10 [group (exposed vs. nonexposed) by trial type (preswitch vs. postswitch) by test trial] mixed ANCOVA, and again controlled for maternal mood by including the HAM-D score as a covariate. There was a significant group (exposure)-by-trial type (preswitch vs. postswitch)-by-trial interaction \( [F(1,31) = 3.56, P = 0.04, \eta^2 = 0.10] \), with no interaction for maternal mood. Follow-up analyses controlling for maternal mood revealed no significant differences in the nonexposed group, but the exposed group showed a significant decline in heart rate between the preswitch and postswitch trials \( [F(1,12) = 6.66, P = 0.024, \eta^2 = 0.36; \text{Fig. 3B}] \).

**Discussion**

This research was designed to examine whether early altered neurochemistry or maternal mental health can change the timing of critical periods in human language development. The results support an accelerated timing of perceptual attunement in SRI-exposed infants; however, postnatal maternal mood also had an impact. Whereas nonexposed infants of control mothers exhibited the typical pattern of discrimination at 6 mo and perceptual narrowing by 10 mo of age, the SRI-exposed infants already showed a more mature pattern, with failure to discriminate nonnative vowel and visual language changes at 6 mo that persisted to 10 mo. Their equivalent behavior to nonexposed fetuses on the vowel discrimination task at 36 wk in utero, coupled with their advanced perceptual capacity on the native consonant discrimination task, further supports an interpretation that failure to discriminate at 6 and 10 mo reflects a generally accelerated development of the speech perception system upon early SRI exposure.

Interestingly, maternal depression had the opposite effect. Infants in this group showed unreliable discrimination at 6 mo, with a tendency toward a familiarity rather than a novelty preference. However, at 10 mo, they reliably discriminated the nonnative sound difference and the change between visual English and visual French. Exposure to maternal depressed mood seems to delay stable discrimination, which ultimately extends the period of sensitivity to nonnative distinctions. Thus, exposure to maternal depression and prenatal SRI exposure appear to exhibit opposite effects on the development of infant speech perception. However, whether this reflects the impact of pre- or postnatal maternal mood remains to be determined.

A mechanistic explication of the biology by which SRIs and maternal depression disrupt critical period timing is essential. One possible explanation is that altered 5-HT levels that result from prolonged gestational antidepressant exposure could change the precision of language representation in the brain. Although direct

<table>
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<th>Characteristic</th>
<th>Nonexposed</th>
<th>SRI-exposed</th>
<th>P value</th>
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<tr>
<td>Education (y)</td>
<td>17.4 ± 2.58</td>
<td>16.57 ± 4.31</td>
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<tr>
<td>HAM-D score (56) at 36 wk gestation</td>
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<td>10.79 ± 3.77</td>
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<td>Smoking (yes/no)</td>
<td>0.07 ± 0.27</td>
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<tr>
<td>Alcohol (no. of drinks for entire pregnancy)</td>
<td>5.1 ± 8.34</td>
<td>4.79 ± 7.63</td>
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<td>Prenatal SRI medications (median mg/d)</td>
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<tr>
<td>Paroxetine</td>
<td>20 ± 0</td>
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<tr>
<td>Fluoxetine</td>
<td>20 ± 0</td>
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<tr>
<td>Sertraline</td>
<td>25 ± 0</td>
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<tr>
<td>Citalopram</td>
<td>30 ± 17.32</td>
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<tr>
<td>Venlafaxine</td>
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<td>36.26 ± 0.37</td>
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<td>Birth gestational age (wk)</td>
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<td>38.78 ± 1.64</td>
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<td>Duration of prenatal SRI exposure (d)</td>
<td>256.67 ± 47.93</td>
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*Significant at \( P < 0.05 \).
human evidence has not been reported, exposure to SRIs early in life has been shown to alter tonotopic organization and receptive field properties in the primary auditory cortex (A1) of rats (15), suggesting that a disruption in auditory coding per se could explain a failure to discriminate speech at 6 and 10 mo by SRI-exposed infants. However, this cannot account for the finding of precocious consonant discrimination in utero by SRI-exposed fetuses. Thus, when all the findings are taken into account, the effect of early SRI exposure appears to be one of accelerated attunement to the properties of the native language.

Emerging reports from animal models suggest that early SRI exposure has a positive influence, reversing or “correcting” the adverse effects of prenatal maternal stress exposure (32–34). Although they are of interest, our results are not entirely consistent with that pattern, as, in our case, SRI exposure appears to lead to an “over-correction.” Below, we discuss how SRI exposure could influence age-related changes in speech perception.

Modulating 5-HT levels increase cortical plasticity in the adult visual system (35, 36). SRIs in particular can reopen cortical plasticity (37), but the means by which they do so has been largely undescribed. Recent insight into the cellular and molecular mechanisms underlying critical period onset and closure in the neocortex of mice now offers a more detailed mechanistic explanation. The maturation of excitatory–inhibitory local circuit balance appears pivotal (11). Any manipulation that ultimately accelerates/delays GABA circuit function will accelerate/delay critical period timing. By analogy, maturational milestones in the auditory system may also reflect a shifted excitatory–inhibitory balance. Apart from the popular action of SRIs on 5-HT transport, these drugs are notorious for their off-target effects (21). Notably, in response to submaximal GABA concentrations, fluoxetine can potentiate current flux through GABA_A receptors containing the α1 subunit (38). Benzodiazepine use early in life is already known to accelerate critical period onset by this mechanism (39).

Turning to the infants of non–SRI-treated but depressed mothers, the compelling finding is their robust discrimination at 10 mo of the nonnative speech sound contrast and the visual language change. This result provides evidence for a delay of the critical period for attunement to the properties of the native language rather than a gross perceptual impairment. An organic difficulty in learning and/or performance on the habituation tasks is one explanation for unreliable discrimination performance at 6 mo. Newborns of depressed mothers show inferior performance on the Brazelton assessment (40, 41), with lower orientation scores, abnormal reflexes, inferior excitability, and withdrawal scores (42). However, the successful discrimination at 10 mo by infants born to depressed mothers not treated with an SRI may be better explained by a delayed critical period trajectory caused by early stimulus deprivation.

By analogy to dark-rearing in the visual system (11), infants of depressed mothers may not hear sufficient speech, or sufficiently engaging speech, to initiate the neurological changes that trigger critical period onset. Depressed mothers do not modify their speaking style (43, 44) to produce the exaggerated “motherese” that infants prefer (45–48), and which can highlight speech sound differences (49). Newborns of depressed mothers fail to show face/voice preference (22) whereas older infants do not learn as well from their mothers’ infant-directed speech (50). Thus, maternal depression may have resulted in subthreshold levels of appropriately engaging speech input. Further support for this possibility is provided by the significant correlation we observed between depression scores at 6 mo and performance in the visual language discrimination task even in control infants.

In summary, we have found that exposure to SRIs accelerates speech perception development, whereas exposure to maternal depression initially disrupts performance and ultimately delays perceptual narrowing by prolonging the period of sensitivity to nonnative distinctions. These findings are particularly compelling when we consider that the timing of speech perception development is typically considered to be maturationally delimited. What is unknown at this time, and of key clinical importance, is whether these small perturbations in critical period timing of core perceptual components of language acquisition have a lasting impact. To date, there are no published reports of language delay in infants or young children with SRI exposure. However, sequential timing and ordered emergence of developing systems is an essential characteristic of optimal development, as it allows more complex processes to build on first established, more foundational representations (51).

We know that, in typical language development, infants use the representations established in native speech sound discrimination to direct later word learning (10) and in rhythmical discrimination to direct later parsing of syntactic units (52). Thus, disruptions in the perceptual foundations of language could have a cascading impact on optimal language development (53). A recent population-level finding reports an intriguing association between prenatal SRI exposure and an increased risk for autism in early childhood (54), raising critical questions (55) about the long-term developmental implications of early mistiming in language development. By providing a deeper mechanistic understanding of how and when developmental trajectories are altered by early exposure to maternal mood disturbances and/or SRI exposure, more optimal outcomes can be realized for infants and their mothers.

**Fig. 3.** Mean fetal heart rate during a speech discrimination task. The $y$ axis represents fetal heart rate in beats per minute (BPM); the $x$ axis represents the 10 preswitch and 10 postswitch trials. Preswitch comprises repeated presentations of the same sound, and postswitch comprises repeated presentations of the changed speech sound ($^*P < 0.05$). (A) SRI-exposed ($n = 14$) and nonexposed ($n = 20$) fetuses at 36 wk gestation in response to a change in vowel sounds /a/-vs. /o/. (B) SRI-exposed ($n = 14$) and nonexposed ($n = 20$) fetuses at 36 wk gestation in response to a change in consonant sounds /da/-vs. /ta/.

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Informed consent was obtained from mothers recruited during their second trimester, and their infants were tested at 36 wk gestation and at 6 mo and 10 mo of age. Mothers were interviewed by trained research assistants using the HAM-D (56) during the second and third trimesters of pregnancy and when their infants were 6 and 10 mo of age. Averages of the prenatal scores were used to classify the 6- and 10-mo-old infants into three groups: no Ss and HAM-D scores <8 (control group), no Ss and HAM-D scores ≥8 (depressed-only group) and SRI-exposed. The HAM-D cutoff score chosen was 8 because scores of 8 to 13 signify mild depression (57).

Auditory Task. A total of 78 infants were tested at 6 mo, and 82 were tested at 10 mo. At 6 mo, participants were excluded for experimenter error (n = 1) and fussiness (n = 6). At 10 mo, participants were excluded for experimenter error (n = 0), fussiness (n = 4), and parental interference (n = 4).

Visual Task. A total of 78 infants were tested at 6 mo, and 80 were tested at 10 mo. At 6 mo, participants were excluded for experimenter error (n = 0), fussiness (n = 11), parental interference (n = 2), failure to habituate (n = 1), and failure to watch the screen (n = 2). At 10 mo, participants were excluded for experimenter error (n = 1), fussiness (n = 16), parental interference (n = 1), failure to habituate (n = 2) and bilingual exposure to French (n = 1).

Fetal Task. Fetuses of 23 mothers treated with an SRI antidepressant agent and 46 non-SRI-treated mothers were tested. Participants were excluded as a result of experimenter error (n = 1 exposed; n = 2 nonexposed), incomplete heart rate signal (n = 4 exposed; n = 7 nonexposed), and fetal movement during the experiment (n = 4 exposed; n = 17 nonexposed). To avoid distortions created by the uterine wall (58), we amplified the low frequency portion of the fetal heart rate signal and used Adobe Audition software to provide partial masking to the stimuli through the state of the fetus. Four states were classified according to the Actocardiograph. The heart rate variability and movement patterns were used to determine the state of the fetuses at the time of testing. This would help to ensure that any effects were a result of stimuli presented and not masked by the state of the fetus. Four states were classified according to the procedure outlined by DiPietro et al. (61). Infants were classified as in quiet sleep (little or no heart rate variability and little or no movements), active sleep (moderate heart rate variability with episodic accelerations and some movements), quiet awake (a rhythmic oscillatory heart rate pattern within a wider bandwidth than quiet sleep and little or no movements), or active awake (high heart rate variability during which accelerations may be fused into tachycardia and movements). The 15 min for the language study was broken into five 3-min blocks. Each 3-min block was analyzed to determine the infant state during that portion.

Stimuli. Hindi sound discrimination. The Hindi dental /da/ and retroflex /da/ syllables were the same as those used by Werker and Lalande (28). They were taken from an eight-step continuum of /da/ sounds created by the Massachusetts Auditory Language Group, which was also used by Weikum et al. (27). The faces of three bilingual (French/English) children were scanned in goldenpath 3D...


