# Serial Structural Imaging in the Postpartum Period Reveals Increases and Decreases in Regional Brain Volumes Following Childbirth

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**Target Audience:** This work will be potentially of interest to those studying puerperal psychosis and postpartum depression.

**Purpose:** To examine the changes that occur in the brain as a result of pregnancy, using state of the art analysis methods. This was an attempt to replicate Oatridge's observation that the brain shrinks during pregnancy [1] and obtain further detail about spatial location. The hypothesis was that by scanning new mothers as soon as possible after birth, and performing longitudinal scanning (time points 0, 2, 4 and 6 months), we would see recovery of brain volume.

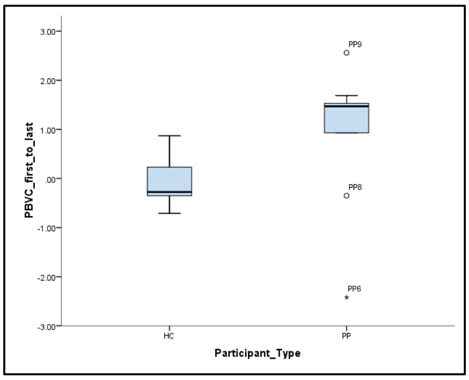
**Method:** Recruitment: Sixteen expectant mothers were initially recruited into the study. However, several mothers had complications during delivery (Caesarean section, heavy bleeding), and several more were slow to adjust to life with a new baby (not leaving the home for several weeks). A glioma was found on the first visit in one mother, and other mothers only attended for one scan. In the end, multiple-time point data were only obtained from 9 mothers. 10 controls (females) were recruited, matched in terms of demographics and age.

Data Acquisition: All data were acquired on a GE 3T HDx system. Structural T1-weighted spoiled gradient recalled echo (SPGR) whole brain image data were collected at 1mm isotropic resolution.

**Data Analysis**: Structural data were initially analysed using SIENA (from the FSL software suite) Initially a standard pair-wise whole brain comparison was performed using SIENA, taking the first and last scan for each participant and computing the percent brain volume change (PBVC).

To provide more detailed anatomical localization of any changes identified, Freesurfer was used to automatically parcellate cortical brain regions, (including estimates of volume and cortical thickness) from 105 distinct regions. Statistical analysis was then performed in R version 2.10.1

**Results:** For the postpartum participants (N =9), the mean PBVC from Siena was 0.89 (i.e. ~1% growth in brain volume), while for healthy controls (N=10), the mean PBVC was -0.12 ((~0.1% reduction in brain volume over time). The figure shows descriptive statistics for the PBVC data in a boxplot (PP = postpartum; HC = Healthy control). As can be seen there was one extreme value in these data: the PBVC for postpartum participant 6, which was -2.42. On trying to understand whether this was an issue with data processing, we noted that this participant had had complications during pregnancy – including pre-eclampsia. If this data point is excluded, then the mean PBVC from first to last scan for postpartum participants is **1.31** (N=8). Between-subjects t-tests showed that the difference between the mean PBVC-first-to-last-scan values for HCs and PPs was non-significant if PP6 was included in the analysis ($t$ = -2.07, df = 9.56, $p$ = 0.08, two-tailed, equal variances not assumed) but was significant if PP6 was excluded ($t$ = -4.33, df = 10.73, $p$ = 0.001, two-tailed, equal variances not assumed).




Longitudinal mixed-effects models [2-6] were applied to quantify the simultaneous linear effects of child age, maternal age at first scan and group (mother v. control) on regional brain volumes and cortical thicknesses. The simultaneous inclusion of variables that could potentially influence brain measurements provides greater precision in the estimates of the effects of each of these predictors [7]. The numbers of subjects available and the numbers of scans per subject were both small, limiting our ability to detect nonlinear relationships, since the identification of more complex functions requires more data points and parameters per subject than those needed to fit simple linear functions [7]. For all analyses, a uniform application of the Akaike Information Criterion [8] determined the inclusion and exclusion of covariates to yield best-fitting yet simplest models among all other choices.

**Table 1 – change in volume / thickness over time**

| Volume | Change over time | # Mothers |
|---|---|---|
| Brainstem | Decreasing | 4 |
| Anterior Cingulate Caudal region (Right) | Decreasing | 5 |
| Anterior Cingulate Rostral Region (Left) | Decreasing | 3 |
| Left hemisphere | Decreasing | 5 |
| Right hemisphere | Decreasing | 5 |
| | | |
| **Cortical Thickness** | | |
| Postcentral gyrus (Right) | Decreasing | 5 |
| Lateral orbitofrontal (right) | Decreasing | 7 |
| Frontal Pole (right) | Increasing | 8 |

Initial data plots and exploratory models revealed an unexpected and increasing relationship between regional volume and date of first scan that is not likely of biological origin. No significant correlation between maternal age and scan date was found. Effects of the unexpected relation were reduced by analyzing % differences between repeated measures relative to the measure at the first scan. Only 9 of the 10 mothers have more than 2 scans after their first. All longitudinal mixed-effects models included group and child age at scan as the only important covariates affecting brain changes over time. Maternal age did not affect measures (subjects were nearly the same age), and was dropped from the models.

Significant postpartum changes in volume were found in 5 brain regions, and in cortical thickness in 3 regions (see Table 1). All postpartum changes differ from those of the control subjects (not shown). For the mothers, on average, eight of the nine regions decreased in volume or thickness over time, and one region increased. The number of mothers whose personal changes were consistent with the average change of the group (who "track") is shown in the final column of Table 1. The numbers of mothers who track varies from three (3/9 =33%) for the volume of the rostral extent of the anterior cingulate cortex in the right hemisphere, to 8 (8/9 = 89%) for the cortical thickness of the frontal pole in the right hemisphere. The region with the least tracking (3/9) shows two precipitous drops, greater than those observed in the other regions. More than one-half of the mothers track in 8 out of 9 regions.

Based on this small sample of postpartum mothers whose brains were measured a small number of times postpartum from near birth to six months, this analysis has identified statistically significant decreases in total brain volume, brainstem, and anterior cingulate cortex bilaterally. Volumetric decreases varied from roughly 2% (total brain volume) to 12% (left hemisphere anterior cingulate volume). Decreases in cortical thickness varied from 4-5%, and an increase of cortical thickness of roughly 15% was seen in the frontal pole.

**Discussion / Conclusion:** In part, this study replicates Oatridge's initial study [1]. However, there were also unexpected *decreases* in gray matter volume / thickness during the postpartum period that demands further investigation. Reliable biological and behavior-cognitive interpretations of the observed brain changes cannot be derived from this pilot study, due to its small sample size, several neuroanatomically regional segmentations, and high residual variability of the repeated measurements after the time trends have been removed. Existing literature lacks solid evidence on connections between brain and behavior in these regions, and in this context, to overcome these technical difficulties.

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