FIGURE S1. Recruitment, Treatment, and Study Assessments

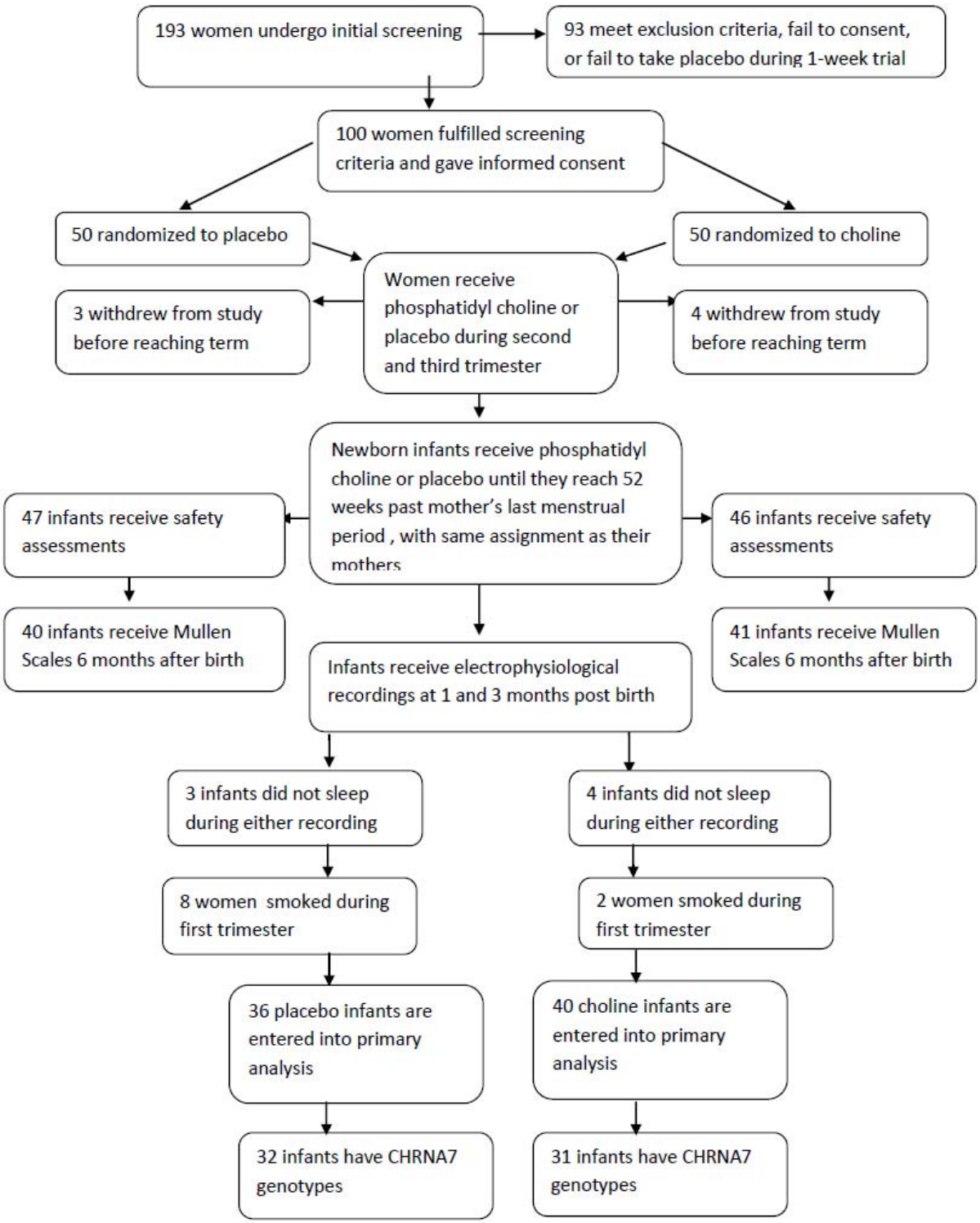

FIGURE S2. Regression of P50 ratio on infant *CHRNA7* genotype. The placebo-treated infants showed a significant correlation of P50 ratio with rs3087454 ($r_s$ = 0.38, df 30, p = 0.032, dashed line). There was no significant correlation for the choline-treated infants (solid line).

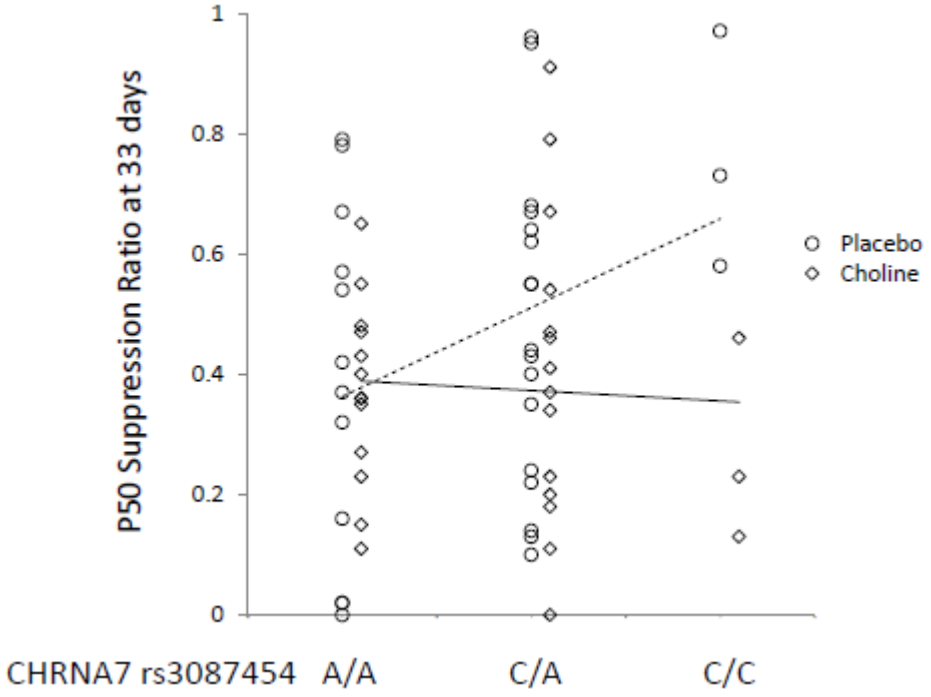

TABLE S1. Parental demographic information for infants recorded electrophysiologically

| | Placebo (N = 36) | | Choline (N = 40) | |
|---|---|---|---|---|
| | Number or Mean | Standard deviation | Number or Mean | Standard deviation |
| Maternal Information | | | | |
| Mother's age | 27.9 | 5.0 | 28.5 | 5.6 |
| Mother's Race/ethnicity | | | | |
| Caucasian Non-Hispanic | 18 | | 18 | |
| Caucasian Hispanic | 13 | | 16 | |
| Mixed or other | 5 | | 6 | |
| Mother's Socio-economic Index | 53.5 | 23.2 | 42.9 | 21.5 |
| Full to partial breast feeding | 29 | | 33 | |
| Prenatal DSM-IV diagnoses | | | | |
| Mood | 2 | | 1 | |
| Anxiety | 4 | | 5 | |
| Psychosis | 1 | | 0 | |
| Prenatal Antidepressants | 3 | | 3 | |
| Paternal Information | | | | |
| Father's age | 29.6 | 5.8 | 28.9 | 6.1 |
| Father's Socio-economic Index | 43.4 | 20.2 | 47.3 | 18.3 |
| Current DSMIV diagnoses | | | | |
| Mood | 2 | | 0 | |
| Anxiety | 2 | | 1 | |
| Psychosis | 1 | | 1 | |

No values are significantly different between placebo and choline treated groups.

The Socio-economic Index (SEI) is based on The Socioeconomic Index of Occupations. 503 occupations are included and are scored in a potential range of 0-100. Managerial, professional, technical, and sales occupations generally have scores above 40; administrative support, service, agricultural, and labor occupations generally have scores below 40. Scores are based on the highest occupation value achieved across an individual's life. A single individual who has never been employed was assigned an SEI score of 0

Nakao K, Treas J. The 1989 socioeconomic index of occupations: construction from the 1989 occupational prestige scores. General Social Survey Methodological Report No. 74. 1992. Chicago, University of Chicago, National Research Center.

TABLE S2. Electrophysiological outcomes

| | Placebo | | Choline | |
|---|---|---|---|---|
| | Mean or number | Standard deviation | Mean | Standard deviation |
| Day 1 | | | | |
| Number recorded | 30 | | 33 | |
| Adjusted age (days) | 34.4 | 8.5 | 31.6 | 4.4 |
| First response: | | | | |
| P50 latency (ms) | 72.8 | 19.9 | 72.5 | 20.8 |
| P50 amplitude (μV) | 2.24 | 1.11 | 2.14 | 1.22 |
| Second response: | | | | |
| P50 latency (ms) | 75.1 | 16.3 | 71.1 | 20.0 |
| P50 amplitude (μV) | 1.14 | 0.88 | 0.90 | 0.68 |
| Ratio of amplitudes | 0.50 | 0.27 | 0.41 | 0.20 |
| | Number | % | Number | % |
| Ratios < 0.5 (%)[1] | 13 | 43% | 25 | 76% |
| Day 2 | | | | |
| Number recorded | 32 | | 33 | |
| Adjusted age (days) | 89.8 | 7.2 | 87.6 | 6.4 |
| First response: | | | | |
| P50 latency (ms) | 75.2 | 18.1 | 71.2 | 15.7 |
| P50 amplitude (μV) | 3.40 | 1.57 | 2.66 | 1.55 |
| Second response: | | | | |
| P50 latency (ms) | 75.1 | 17.7 | 71.7 | 15.8 |
| P50 amplitude (μV) | 1.25 | 0.81 | 1.06 | 0.84 |
| Ratio of amplitudes | 0.39 | 0.24 | 0.39 | 0.25 |
| | Number | % | Number | % |
| Ratios < 0.5 (%) | 23 | 72% | 25 | 76% |

[1] $\chi^2 = 6.90$, df 1, $P = 0.009$. No other comparisons showed significant differences.

**TABLE S3. Exploratory subgroup analyses of infant P50 ratio**

| Day 1 | Placebo | | | Choline | | | |
|---|---|---|---|---|---|---|---|
| **Number of infants by P50 ratio:** | **<0.5** | **≥0.5** | **% <0.5** | **<0.5** | **≥0.5** | **% <.05** | **Fisher p** |
| Primary outcome (excludes smokers) | 13 | 17 | 43 | 25 | 8 | 76 | 0.011 |
| Smokers included | 18 | 18 | 50 | 25 | 8 | 76 | 0.046 |
| P50 recordings on both days | 11 | 15 | 42 | 17 | 8 | 68 | 0.093 |
| Maternal SEI > 40 | 9 | 8 | 53 | 13 | 1 | 93 | 0.021 |
| Maternal SEI < 40 | 4 | 8 | 33 | 10 | 7 | 59 | 0.26 |
| No parental diagnosis of mental disorder | 4 | 6 | 40 | 11 | 3 | 79 | 0.092 |
| No maternal antidepressants | 10 | 16 | 38 | 20 | 7 | 74 | 0.013 |

| Day 2 | Placebo | | | Choline | | | |
|---|---|---|---|---|---|---|---|
| **Number of infants by P50 ratio:** | **<.5** | **>=.5** | **% <.5** | **<.5** | **>=.5** | **% <.5** | **Fisher p** |
| Primary outcome (excludes smokers) | 23 | 9 | 72 | 25 | 8 | 76 | 0.78 |
| Smokers included | 23 | 14 | 62 | 25 | 9 | 74 | 0.32 |
| P50 recordings on both days | 17 | 9 | 65 | 19 | 6 | 76 | 0.054 |
| Maternal SEI > 40 | 10 | 7 | 59 | 10 | 1 | 91 | 0.099 |
| Maternal SEI < 40 | 11 | 2 | 85 | 14 | 7 | 67 | 0.43 |
| No parental diagnosis of mental disorder | 7 | 5 | 58 | 15 | 1 | 94 | 0.057 |
| No maternal antidepressants | 20 | 9 | 69 | 22 | 7 | 24 | 0.77 |

| Correlation with CHRNA7 rs3087454 (day 1) | Mother's SEI | Maternal antenatal antide-pressant | Maternal smoking in 1st trimester | Maternal antenatal mood or anxiety disorder | Parental lifetime mental disorder | Infant recorded at both times | Rank correla-tion with genotype |
|---|---|---|---|---|---|---|---|
| **All genotyped infants** | | | | | | | |
| Placebo n = 33 | | | | | | | |
| Number or mean | 52 | 3 | 5 | 4 | 22 | 25 | 0.38 |
| % or S.D. | 22 | 9 | 16 | 12 | 69 | 76 | |
| Choline n = 29 | | | | | | | |
| Number or mean | 46 | 4 | 0 | 4 | 16 | 25 | -0.05 |
| % or S.D. | 22 | 14 | 0 | 14 | 55 | 86 | |
| **No antenatal exposure to smoking and antidepressants** | | | | | | | |
| Placebo n = 24 | | | | | | | |
| Number or mean | 52 | -- | -- | 4 | 15 | 22 | 0.29 |
| % or S.D. | 23 | -- | -- | 17 | 62 | 92 | |
| Choline n = 24 | | | | | | | |
| Number or mean | 46 | -- | -- | 3 | 12 | 22 | 0.09 |
| % or S.D. | 21 | -- | -- | 12 | 50 | 92 | |
| **CHRNA7 rs3087454 C/C homozygotes, individual values** | | | | | | | **P50 ratio** |
| Placebo n = 3 | 43 | 0 | 0 | 1 | 1 | 1 | 53 |
| | 53 | 0 | 0 | 0 | 0 | 0 | 73 |
| | 73 | 0 | 0 | 0 | 1 | 1 | 97 |
| Choline n = 3 | 36 | 0 | 0 | 0 | 1 | 1 | 13 |
| | 30 | 0 | 0 | 0 | 1 | 1 | 23 |
| | 38 | 0 | 0 | 0 | 0 | 1 | 46 |

## Supplementary Methods

### Electrophysiological recording

Newborns are uncooperative during waking and therefore the recordings are performed during active sleep, the infant analogue of Rapid Eye Movement (REM) sleep. This unconscious hypotonic state makes highly reproducible recordings possible. Although adult electrophysiological recordings are generally performed during waking, the differences between normals and patients with schizophrenia also occur during REM sleep (1). Vertex electroencephalogram, electrooculogram, submental electromyogram, and respiration were recorded continuously while infants slept. Pairs of auditory clicks with 85 dB sound pressure level and 0.5 sec intrapair interval were delivered every 10 sec. Sleep state was identified offline, and average waveforms were computed from the first 15 minutes of active sleep (2). P50 has 70 ms latency in newborns. The amplitude of the largest positivity between 50 and 100 ms following each click and preceded by a negative trough was determined by an investigator blinded to infant identity and treatment. Sensory gating was measured as the P50 suppression ratio, the average amplitude of P50 evoked by the second click divided by the average amplitude of the response to the first click (Figure 1A). Correlation of this measure in infants over 1 week is r = 0.86 (3).

### *CHRNA7* genotypes

DNA samples amplified from cheek swabs from 62 infants were genotyped at a single nucleotide polymorphism rs3087454 A/C in the *CHRNA7* promoter, 1831 base pairs 5' of Exon 1, which has been informative in schizophrenia (4). For Caucasians, the minor C allele (f = 0.36)

is associated with schizophrenia, and for African-Americans, the A allele is associated. One African American was genotyped in the present sample; the infant's genotype was excluded from further analysis because of the racial difference in association of this genotype with schizophrenia. The genotype effect was assessed by a Spearman's rho correlation ($r_s$) of P50 ratio to the three possible genotypes for each treatment group.

**References**


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