To appear in the *Proceedings of the 32nd Annual Boston University Conference on Language Development*

.

Prenatal Glucocorticosteroids Selectively Impair Language Development

Karin Stromswold
Rutgers University – New Brunswick

Abstract. Prenatal exposure to excessive amounts of glucocorticosteroids (GCs) adversely affects the neural development and subsequent behavior of animals (see Matthews, 2000). Despite this, women who are likely to delivery prematurely are routinely given prenatal GCs because they decrease morbidity and mortality in preterm (PT) infants. Between 1994 and 2000, there was no consensus about the optimal number of courses of GCs to give and, consequently, clinically similar pregnant women received different amounts. We took advantage of this natural experiment and investigated the impact of prenatal GCs on the development of 495 PT children and 481 full-term (FT) children who had risk factors for being born prematurely. Of the PT children, 47% received no courses of GCs, 33% received 1 course, 9% received 2 courses, and 10% received 3 or more courses (range 3-12). Of the FT children, 58% received no courses of GCs, 28% received 1 course, 6% received 2 courses, and 8% received 3 or more courses (range 3-11). Based on the animal findings, we predicted that children who received more GCs would have significantly poorer outcomes than those who received less GCs. For the PT children, there was a significant linear relationship between GCs and poorer outcome for 70% of the linguistic measures, but only 5% of the nonlinguistic outcome measures. A similar pattern was observed for the FT children, with 3 or more courses of GCs resulting in significantly worse outcome for 75% of the linguistic measures. We discuss reasons why language development appears to be more vulnerable to prenatal GCs than other areas of development.

Prenatal Glucocorticosteroids Selectively Impair Language Development

Karin Stromswold
Rutgers University – New Brunswick

1. Introduction

Language development in perinatally high-risk children. As a group, children who are born prematurely (PT, before 37 weeks gestation) reach language milestones later, perform more poorly on a wide range of language tests, and are more likely to be diagnosed with language disorders than their full-term (FT) peers (see, for example, Taylor, Klein, & Hack, 2000; Taylor, Klein, Minich et al., 2000, and references therein). These studies reveal that the more premature the child, the greater the risk of poor linguistic skills, but that even children born between 32 and 36 weeks gestation do more poorly than children born FT (Hediger et al., 2002; Huddy et al., 2001). Even PT children with normal cognitive function and no major neurodevelopmental disability are 2 to 3 times more likely to be language impaired than FT children. Low birth weight (BW) is a risk factor for linguistic delays and impairments independent of prematurity. For example, even low BW children who are FT are more likely to suffer from language and learning impairments than FT normal BW children (Low et al., 1992; Walther, 1988). Multivariate regression analyses reveal a significant positive relationship between BW and performance on a variety of linguistic tasks even at BWs above 3000 grams (Breslau et al., 1996; 2000). Even FT low BW children who are apparently neurologically intact do worse on language tasks than normal BW children (Breslau et al., 1996; 2000; Low et al., 1992; Walther, 1988). Lastly, twins are 2 to 3 times more likely be language impaired than singletons, and even linguistically normal twins' language lags 2 to 3 months behind that of singletons (see Stromswold, 2006c).

Although many studies have shown that children who are born PT, low BW and/or are twins are at increased risk for language delays and disorders, few studies have carefully investigated why this is so. This paper investigates whether excess perinatal GCs are (in part) responsible for their linguistic delays.

Neurodevelopmental effects of excess perinatal GCs. Many studies have shown that animals exposed to excessive GCs perinatally often have structural and functional brain abnormalities (see Matthews, 2000). For example, at 20 months of age, rhesus monkeys exposed to one prenatal course of GCs have a 30% reduction in hippocampal volume (Uno et al., 1994), and rats exposed to

This work was supported by grants from NSF (BCS-0446838), the Busch Biomedical Research Fund, and the Bamford-Lahey Children's Foundation. I am indebted to Diane Molnar, Ellyn Sheffield, a small army of research assistants, and the parents and children who participated in the PEGI study. I am also grateful to members of the audience of the 32nd Boston University Conference on Language Development for their insightful comments and suggestions. Correspondence may be sent to karin@ruccs.rutgers.edu.

GCs neonatally do poorly on T-mazes in a way that suggests impairment of higher cognitive functions (Golub, 1982). The consensus is that the effects of GCs depend on the amount of GCs given (higher or repeated doses are worse), the age of the animal at the time of administration (GC exposure during the second half of gestation is generally worse), and the species tested (animals that give birth to immature young are typically more affected).

PT infants are frequently given neonatal GCs improve their respiratory function. Most studies have shown that children who receive neonatal GCs have smaller head circumferences and brain volumes (see Parikh et al., 2007) and are 2 to 3 times more likely to have major neurodevelopmental impairments than PT children who do not receive neonatal GCs (see O'Shea et al., 2007).

Prenatal GCs also improve respiratory function in PT children, and several studies suggest that PT children who receive a single course of prenatal GCs have as good cognitive outcome as PT children who received no prenatal GCs (see Dalziel et al., 2005 and references therein). Because of this, in 1994, NIH recommended all women threatening to deliver prematurely receive prenatal GCs (NIH Consensus Development Conference, 1994). However, NIH did not say what the optimal number of GCs courses was, and consequently, obstetricians began giving differing amounts of GCs. Soon thereafter, French et al. (1999) reported that preterm children exposed to 3 or more courses of prenatal GCs were more hyperactive and aggressive than those exposed to 2 or fewer courses, and Esplin (2000) reported that infants exposed to multiple courses of prenatal GCs had more cognitive and psychomotor delays than those exposed to a single course, In response, in 2000, NIH officially discouraging multiple courses of prenatal GCs (NIH Consensus Development Conference, 2000). Subsequent studies have yielded mixed results. Kumar et al (2004) found no difference between preterm toddlers exposed to one vs. multiple courses of prenatal GCs. In two larger studies, Crowther et al. (2007) and Wapner et al. (2007) also found that, with respect to major neurodevelopmental impairments, there was no difference between toddlers who received single vs. multiple courses of prenatal GCs. However, Crowther et al. (2007) found that toddlers who received multiple courses of prenatal GCs had more attentional problems, and Wapner et al. (2007) found that toddlers who received 4 or more courses of prenatal GCs were more likely to die or have cerebral palsy.

2. Study 1: Prenatal GCs and Preterm Children's Development

To date, no studies have studied the effect of multiple courses of GCs on language development. Because between 1994 and 2000, there was no consensus about the optimal GC dosage, clinically similar pregnant women received different amounts of GCs. We took advantage of this to investigate the impact of prenatal GCs on language development. By comparing the abilities of PT children exposed to differing amounts of prenatal GCs, we sought to tease apart which linguistic deficits are specifically the result of GC exposure and which are the results of other factors associated with being born prematurely

PT Participants. The participants in the study were PT children in our

Perinatal Environment and Genetic Interactions (PEGI) study whose parents knew how much prenatal GCs they received. Because many studies how shown that the development of PT and FT children differs (see above), we analyzed PT and FT children's data separately. Four hundred ninety-five PT children participated in the study, with 52% being male. Eighty percent of the children were twins, and 20% were singletons. At the time of assessment, the PT children's mean age (corrected for prematurity) was 41.8 months (SD = 26.0 months). Their mean BW was 1910 grams (SD = 645 grams), with 13% being born extremely low BW (< 1000 g), 7% being very low BW (1000-1500 g), 44% being low BW (1500-2500 g), and 18% being born normal BW (> 2500 g). Their mean gestational age at birth (GA) was 32.8 weeks (SD = 3.3 weeks), with 13% being born before 29 weeks GA, 10% being born between 29 and 32 weeks GA, and 66% being born between 33 and 36 weeks. Forty-seven percent of the PT chilren received no courses of GCs, 33% received 1 course, 9% received 2 courses, and 10% received more than 2 courses (range 3-12).

Language Outcome Measures. We analyzed the impact of prenatal GCs on 13 measures of linguistic development. The first type of measure was scores on parent-administered language tests. Scores on the Ages and Stages (AS) communication test (Bricker et al., 1999) were used to assess overall communicative ability. Unfortunately, the AS communication test does not assess different components of language separately. Because no parent-administered test existed that does so, we created the Parent Assessment of Language test (Stromswold, 2003, 2006a). [1]

In the PAL, articulation is assessed by a word repetition task in which parents judge whether children correctly say the consonant or consonant cluster onset of 12 words (e.g., the <u>r</u> in *rat*, the <u>fr</u> in *frog*). Lexical access is assessed by a standard rapid naming test (e.g., name as many animals as you can in 30 seconds) and by a "name quickly" task in which children are asked to generate words that meet particular requirements (e.g., name a part of a face). Syntax is

[1] Results of several studies indicate that PAL scores are excellent measures of preschool children's linguistic abilities. In the first study (Stromswold, 2006b), PAL data from 688 preschool children (ages 36 to 71 months) who participated in the PEGI study revealed that PAL scores were significantly correlated with all other language measures (all p's < .0001), with the median correlation between PAL Oral scores and scores on other language measures being .55 (p < .0001). PAL Oral scores were also very good at identifying children with language impairments (area under the Receiver Operating Characteristic curve = 0.86). In a second study (Stromswold, 2006b), 20 preschool children took the PAL, Denver Articulation Screening Examination (DASE, Drumwright, 1971) and the Clinical Evaluation of Language Fundamentals-Preschool test (CELF-P, Wiig et al., 1992). PAL Articulation and DASE scores were highly correlated (r = .66, p < .001), as were composite PAL scores and composite CELF scores (r = 70, p < .001) . In a third study (Stromswold et al., 2006), 122 children took the PAL, DASE and revised version of the CELF-P (CELF-P2, Wiig et al., 2004). The correlation between PAL Articulation and DASE scores was .42 (p < .0001) and between composite PAL and composite CELF-P2 scores was .74 (p < .0001), with PAL Oral scores being excellent at identifying children with language impairments (area under ROC curve = .96).

assessed by a forced-choice, picture-pointing comprehension test of sentences that contain reflexive pronouns (e.g., *himself*), accusative pronouns (e.g., *him*), and semantically reversible active and passive sentences. A measure of overall oral language skills was obtained by adding the Z-scores of PAL articulation, lexical access and syntax scores (PAL Oral score). Lastly, children's pre-reading skills are assessed via a letter recognition task and older children's reading skills are assessed via a single word reading task. (For a sample PAL, see http://ruccs.rutgers.edu/~karin/PERINATAL/PALS/PAL4.pdf.)

We also analyzed children's scores on 7 parent-report language measures. Parents reported when their child achieved 4 language milestones (babbling, first word, first multiword utterance, articulating clearly enough that strangers could understand the child). Parents rated on a 5-point scale how their child's linguistic abilities compare to those of children the same age (comparative language skills). Parents also reported whether their child received speech-language therapy (SLT) during each year of life. Thirty percent the PT children received some SLT. We calculated the amount of SLT received by dividing the number of years of therapy divided by the child's age. The mean amount of SLT/age was 0.22 (range 0-1). Lastly, starting in 2006, parents completed the Children's Communication Checklist (CCC-2, Bishop, 2006)

Nonlinguistic Outcome Measures. We also analyzed the impact of prenatal GCs on children's non-linguistic development. Our 8 gross motor measures were AS gross motor scores, onset of 5 gross motor milestones (sitting, crawling, walking, climbing stairs and running), comparative gross motor skills, and amount of physical therapy received. Our 7 fine motor measures were AS fine motor scores, onset of 4 fine motor milestones (finger feeding, using a spoon or fork, scribbling, and cutting with scissors), comparative fine motor skills, and amount of occupational therapy received. Our 4 social development measures were AS social/personal scores, onset of social smiling, comparative social skills, and amount of psychological/behavioral therapy received. Our 3 cognitive measures were AS problem solving scores, comparative cognitive skills, and amount of special education services received. Lastly, our 2 oral motor measures were onset of drinking from an open cup and amount of feeding therapy received.

Predictions. Both animal and human results predict that PT children who received the most GCs will have the worst outcome. The studies make different predictions about the impact of smaller doses. Animal studies have generally shown a steady decline in performance with increasing doses of GCs, which leads to the prediction that PT children who received 3 or more courses of GCs will have worse outcomes than those who received 2 courses who in turn will have worse outcomes than those who received a 1 course. This model was tested using linear contrast ANOVAs (contrast weights: no GCs = +3, 1 course = +1, 2 courses = -1, more than 2 courses = -3). Several studies of PT children have found that PT children who received more than 2 courses have poorer outcome than those who received fewer (or no) courses of GCs. This "L-shaped" model was tested using non-linear contrast ANOVAs (contrast weights:

no GCs = +1, 1 course = +1, 2 courses = +1, > 2 courses = -3).

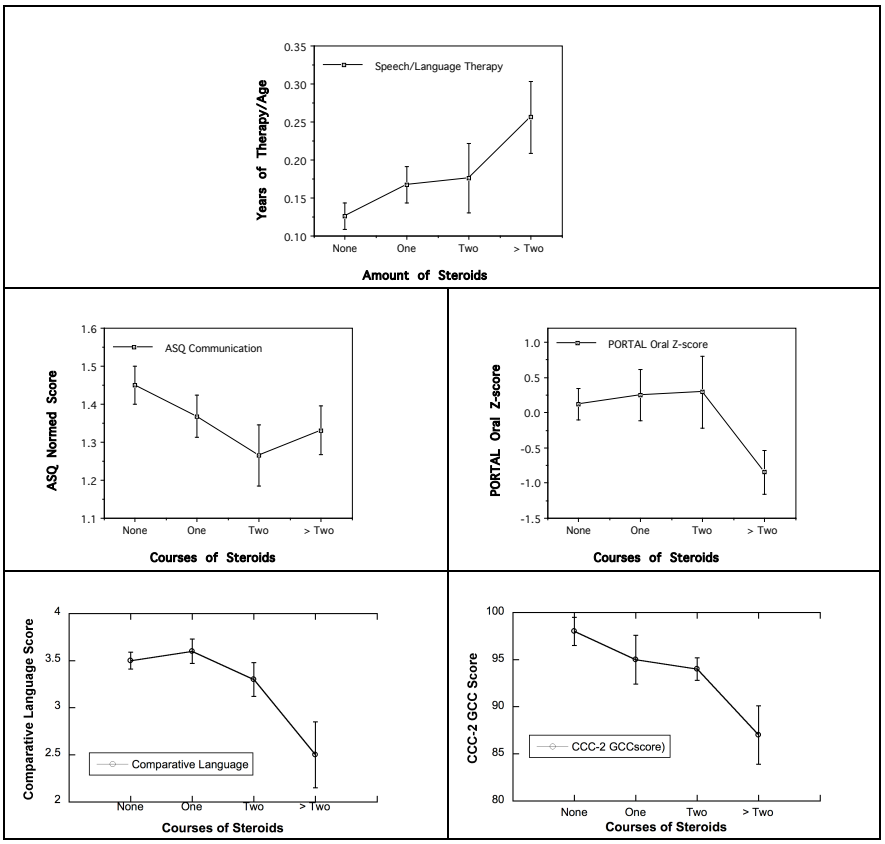

Figure 1. Effect of GCs on PT Children's Overall Language Development

Prenatal GCs and Linguistic Outcome. Figure 1 depicts how the amount of GC affected overall linguistic ability. Linear contrast ANOVAs revealed a significant effect of GCs in the predicted direction for all 5 measures of overall linguistic ability (SLT $F(1, 488) = 10.62$, $p = 0.001$; AS Communication $F(1, 329) = 3.72$, $p = 0.05$; PAL Oral Z-score $F(1, 225) = 5.43$, $p = .02$; Comparative Language $F(1, 355) = 3.70$, $p = 0.05$; CCC-2 scores $F(1, 245) = 3.89$, $p = 0.05$). L-shaped contrast ANOVAs revealed a significant GC effect for 4 of these measures (SLT $F(1, 488) = 5.39$, p = .02; PAL Oral Z-score $F(1, 225) = 7.00$, $p = .009$; Comparative Language $F(1, 355) = 3.73$, $p = 0.5$; CCC-2 scores $F(1, 245) = 3.51$, $p = 0.06$). Figure 2 depicts how amount of GCs affected different aspects of language tested in the PAL. There was a significant linear GC effect for lexical access scores ($F(1, 225) = 7.45$, $p = 0.007$), syntax scores ($F(1, 225) = 5.70$, $p = 0.02$) and literacy scores ($F(1, 225) = 4.39$, $p = .04$). The L-shaped contrast ANOVAs yielded very similar results (lexical access $F(1, 225) = 6.34$,

p = .01; syntax $F(1, 225) = 6.92$, p = .009; literacy $F(1, 225) = 3.33$, p = .07).

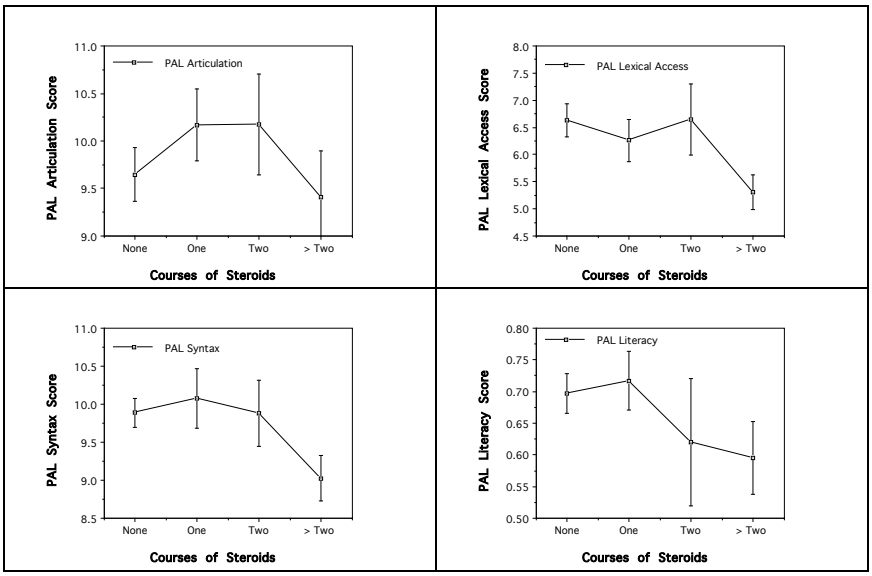

Figure 2. Effect of GCs on PT Children's Scores on PAL Subtests

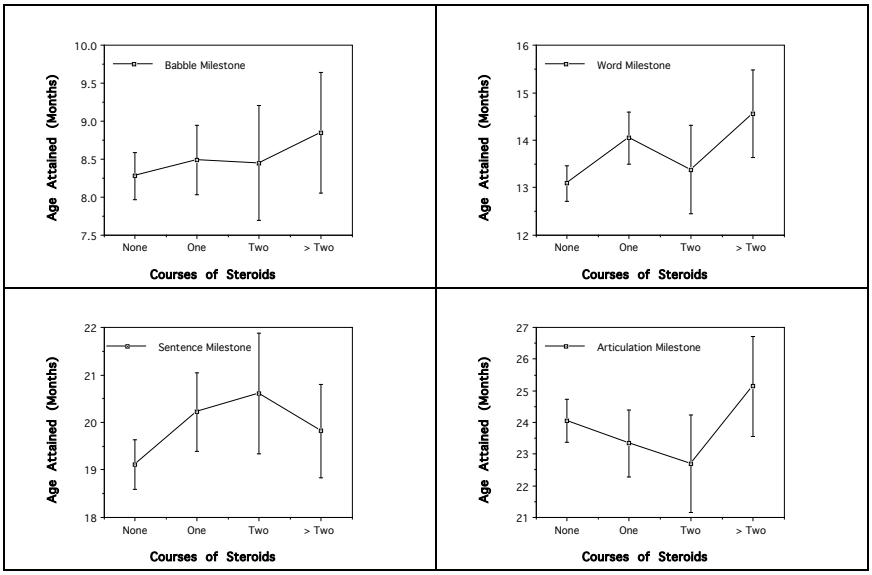

Figure 3. Effect of GCs on PT Children's Onset of Language Milestones

Figure 3 depicts the relationship between amount of GCs and age of acquisition of language milestones. Linear ANOVAs revealed a marginally significant GC

effect for onset of words ($F(1, 327) = 3.05$, $p = 0.08$), whereas the L-shaped ANOVAs revealed no GC effect for any of the language milestones.

Prenatal GCs and Nonlinguistic Outcome. In striking contrast to the results for linguistic outcome measures, contrast ANOVAs of the non-linguistic outcome data revealed no GCs effect for 22 of the 24 measures of nonlinguistic development. However, as depicted in Figure 4, both contrast ANOVAs revealed a significant effect in the predicted direction for psychological/behavior therapy (linear contrast $F(1, 488) = 4.82$, $p = .03$; L-shaped contrast $F(1, 488 = 4.57$, $p = .03$). Contrast ANOVAs also revealed a significant GC effect for AS problem solving scores (linear contrast $F(1, 328) = 9.06$, $p = .003$; L-shaped contrast $F(1, 488) = 4.57$, $p = .026$). However, inspection of Figure 4 reveals that the GC effect was in the opposite direction from that which was predicted, with children who received more GCs having better AS problem solving scores.

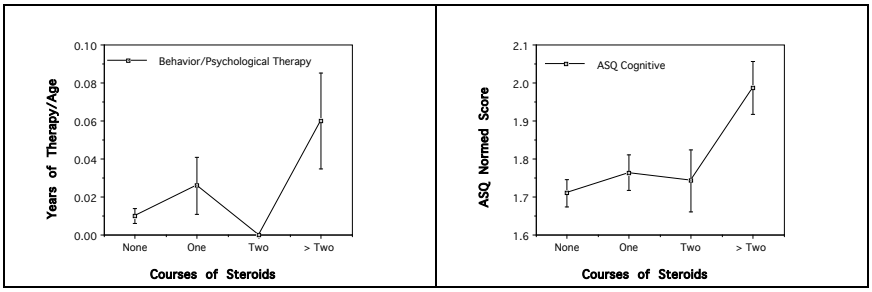

Figure 4. Effect of GCs on PT Children's Nonlinguistic Development

3. Study 2: Prenatal GCs and Full-term Children's Development

Approximately 25% of pregnancies have risk factors for PT delivery (Beck, 1989), yet only 11% of infants are born PT. Thus, one way to tease apart the effects of prenatal GCs from other factors associated with prematurity is to study high-risk children with prenatal exposure to GCs who were born FT.

Full-term Participants. We investigated the impact of prenatal GCs on linguistic and nonlinguistic outcome of 481 PEGI children who were FT (GA at birth > 36 weeks). Forty-nine percent of the FT participants were male. Ninety-four percent were twins and 6% were singletons. At the time of assessment, their mean age (adjusted for weeks born prior to 40 weeks) was 38.8 months (SD = 26.9). Their mean BW was 2820 grams (SD = 441 grams) and their mean GA was 37.9 weeks (SD = 1.0 week). Fifty-eight percent received no courses of GCs, 28% received one course, 6% received two courses, and 8% received 3 or more courses (range 3-11). Consistent with previous studies, fewer FT children received SLT than PT children (17% vs. 30%, respectively) and FT children received less SLT than PT children (0.09 years/age vs. 0.22 years/age).

Results. The same outcome measures and ANOVAs that were used in the first study were used in this study. Due to space limitations, we will only discuss the effect of GCs on FT children's language. Figure 5 depicts how

amount of GC affected FT children's scores on 4 measures of overall linguistic ability. Linear contrast ANOVAs revealed a significant linear effect of GCs in the predicted direction for amount of SLP received ($F(1, 477) = 14.55$, $p = .0002$), and a marginally significant effect for AS communication scores ($F(1, 457) = 3.02$, $p = .08$) and PAL Oral Z-scores ($F(1, 321) = 3.40$, $p = .07$). L-shaped contrast ANOVAs revealed a significant GC effect for SLT ($F(1, 477) = 17.54$, $p = .00003$), AS communication scores ($F(1, 457) = 5.68$, $p = .02$) and PAL Oral Z-scores ($F(1, 321) = 11.92$, $p = .0006$). In contrast with the finding for PT children, there was no significant linear or L-shaped GC effect for FT children's comparative language ratings (both p's > .10).

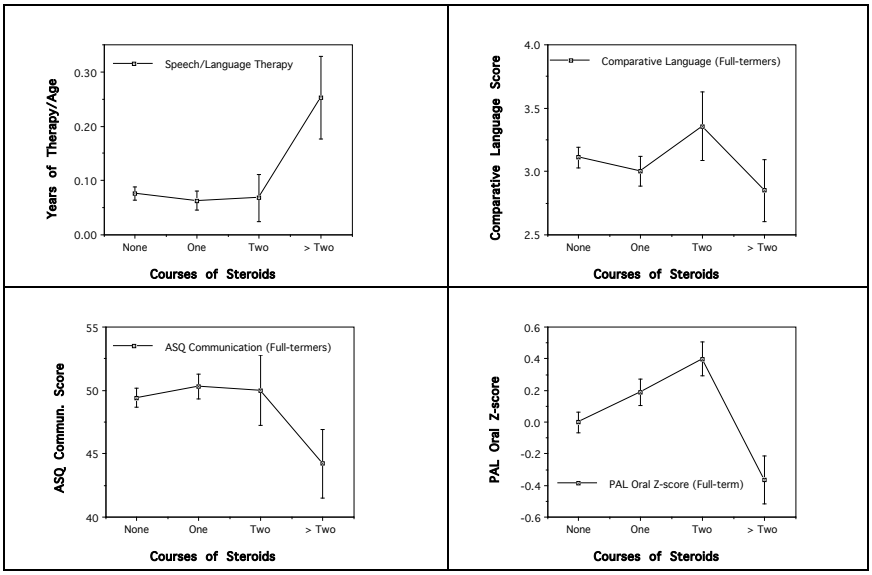

Figure 5. Effect of GCs on FT Children's Overall Language Development

Figure 6 depicts how amount of GCs affected FT children's performance on the 4 PAL subtests. There was only a linear GC effect for PAL lexical access scores ($F(1, 321) = 7.09$, $p = 0.081$). In contrast, L-shaped contrast ANOVAs revealed significant GC effects for FT children's PAL lexical access scores ($F(1, 321) = 10.64$, $p = .001$), syntax scores ($F(1, 321) = 5.01$, $p = .03$), and literacy scores $F(1, 321) = 3.90$, $p = .06$). Lastly, Figure 7 depicts the relationship between how much GCs FT children received and when they acquired 4 language milestones. There was a significant linear GC effect for onset of babbling ($F(1, 358) = 8.16$, $p = .005$) and a marginally significant effect for onset of words ($F(1, 382) = 3.48$, $p = 0.06$). There was a significant L-shaped effect of GCs for onset of babbling ($F(1, 358) = 11.74$, $p = .0007$), words ($F(1, 382) = 8.72$, $p = .003$) and sentences ($F(1, 306) = 6.31$, $p = .01$).

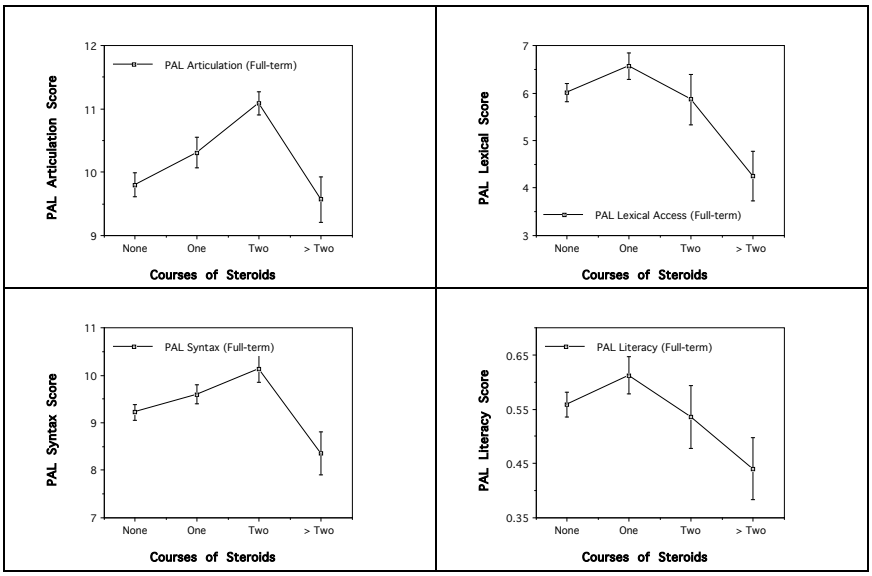

Figure 6. Effect of GCs on FT Children's Scores on PAL Subtests

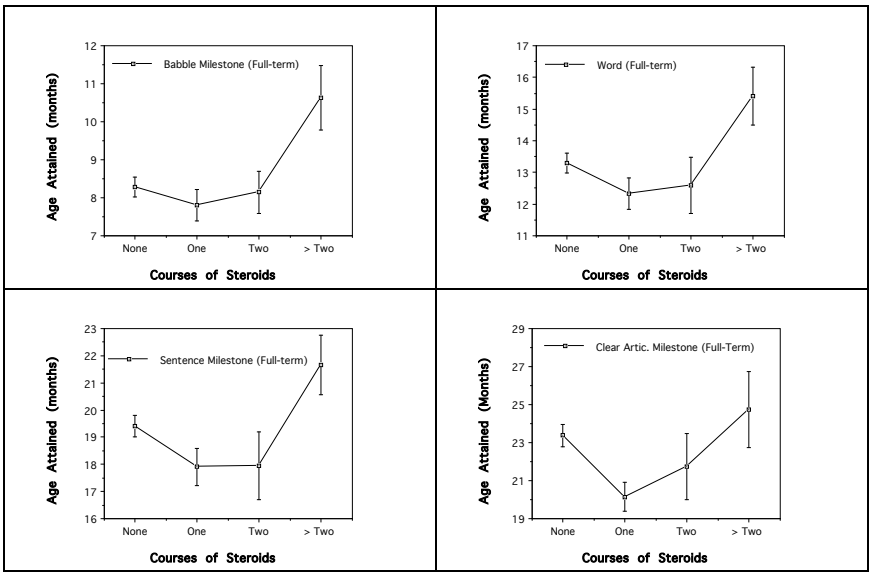

Figure 7. Effect of GCs on FT Children's Onset of Language Milestones

4. Summary and Discussion

To summarize, for PT children, linear contrast ANOVAs revealed a significant or marginally significant linear effect of prenatal GCs for 70% of PT children's language measures (8 significant, 1 marginally significant), and L-

shaped contrast ANOVAs revealed a significant or marginally significant L-shaped effect of prenatal GCs effect for 50% of their language measures (6 significant, 1 marginally significant). For FT children, linear contrast ANOVAs revealed a significant or marginally significant linear effect of prenatal GCs for 50% of the FT children's language measures (3 significant, 3 marginally significant), and L-shaped contrast ANOVAs revealed a significant L-shaped effect for 75% of their language measures. These findings suggest that both PT and FT children's brains are vulnerable to the adverse effects of GCs. Furthermore, the fact that maternal cortisol levels are elevated in virtually all high-risk pregnancies may explain why prematurity, low BW, multiple gestation pregnancies and intrauterine infection are risk factors for developmental delays.

A notable difference between the PT and FT children's findings is that, the linear model fit the PT children's language data better than the L-shaped model, and the L-shaped model fit the FT children's language data better than the linear model. One possible explanation for this is that most PT children face a panoply of neurological insults postnatally, and these insults make the PT child's brain vulnerable to even low doses of GCs (Stromswold, 2006c). The FT child's brain – which doesn't suffer these additional insults – is relatively resilient and only very high doses of prenatal GCs result in linguistic deficits.

Both PT and FT children, prenatal GCs appear to affect linguistic outcome more than nonlinguistic outcome. The million dollar question is, why is this so? Perhaps language is not more vulnerable to prenatal GCs. For example, prenatal GCs might be confounded with other perinatal risk factors. However, this wouldn't explain why GCs affect linguistic development more than nonlinguistic development, nor would it explain why FT children's language is also affected. Another possibility is that prenatal GCs are confounded with postnatal social factors. However, this seems unlikely because the amount of prenatal GCs that women received didn't vary systematically with factors such as SES. Language development might be an indicator of subtle, nonspecific developmental delays. Yet another possibility is that impairments in many different domains can cause language impairments. However, this explanation is problematic because, with the possible exception of social development, GCs didn't appear to affect nonlinguistic development. Finally, weakness in several nonlinguistic domains (that are not detected by our measures) might interact synergistically to cause detectable linguistic delays.

Although children with frank hearing losses were excluded from this study, what appears to be a language-specific effect of GCs may be due to subtle GC-induced hearing loss. Rats exposed to prenatal GCs have subtle hearing losses (Kadner et al., 2006). Furthermore, PT infants are frequently jaundiced, and bilirubin's ototoxic effects are magnified by GCs. PT infants also spend the first weeks of life in noisy neonatal intensive care units, and GCs make hair cells more vulnerable to noise-induced death (Kadner et al., 2006).

Language development might really be more vulnerable to excess prenatal GCs. Rats exposed to excess prenatal GCs have structural abnormalities in the auditory cortex (Canlon et al., 2006), which raises the possibility that other

language-related regions are particularly vulnerable to prenatal GCs. Prenatal GCs interfere with DNA, RNA and protein synthesis, thereby affecting neuronal migration, differentiation, myelination, and dendritic and axon growth and pruning, with GCs having greater impact during certain phases of these processes (Matthews, 2000). Pregnant women most often receive GCs between 29 and 33 weeks GA and, during this interval, neurons in the "language" brain regions may be more vulnerable to the epigenetic effects of excess GCs than other regions of the brain are. Lastly, because perisylvian language areas are in a vascular watershed, they are particularly vulnerable to hypoxic/ischemic injury. This, coupled with the fact that prenatal exposure to GCs potentiates the effects of hypoxia and increases the risk of hypoxic brain injury during the neonatal period (Carlos, Seidler & Slotkin, 1991), could explain why prenatal GCs preferentially hurts language development. Although the studies presented in this paper can't explain why GCs selectively impairs language development, the fact that this appears to be the case provides a novel type of evidence for the neurodevelopmental and functional modularity of language.

References

Beck, W. W. J. (1989). *Obstetrics & gynecology, 2nd ed*. New York City: John Wiley.

Bishop, D. V. M. (2006). *The Children's Communication Checklist-2, United States edition*. San Antonio, TX: Harcourt Assessment, Inc.

Breslau, N., et al. (1996). Low birth weight and neurocognitive status at six years of age. *Biological Psychiatry, 40*(5), 389-397.

Breslau, N., et al. (2000). Neurologic soft signs and low birthweight: Their association and neuropsychiatric implications. *Biological Psychiatry, 47*(1), 71-79.

Bricker, D., & Squires, J. (1999). *Ages & Stages Questionnaire: A parent-completed, child-monitoring system, second edition*: Paul H. Brookes Publishing Company.

Canlon, B., et al. (2003). Alterations in the intrauterine environment by glucocorticoids modifies the development programme of the auditory system. *European Journal of Neuroscience, 17*, 2035-2041.

Carlos, R. Q., Seidler, F. J., & Slotkin, T. A. (1991). Fetal dexamethasone exposure sensitizes neonatal rat brain to hypoxia: Effects on protein and DNA synthesis. *Brain Research. Developmental Brain Research, 64*(1-2), 161-166.

Crowther, C. A., et al. (2007). Outcomes at 2 years of age after repeat doses of antenatal corticosteroids. *New England Journal of Medicine, 357*(12), 1179-1189.

Dalziel, S. R., et al. (2005). Antenatal exposure to betamethasone: Psychological functioning and health related quality of life 31 years after inclusion in randomised controlled trial [Electronic Version]. *BMJ*, 331. Retrieved August 2006.

Drumwright, A. (1971). *Denver Articulation Screening Examination*. Denver, CO: University of Colorado Medical Center.

Esplin, S. (2000). *Long-term outcome after repeated courses:* Paper presented at the Antenatal Corticosteroids: Repeat Courses Conference, Bethesda MD.

French, N. P., et al. (1999). Repeated antenatal corticosteroids: Size at birth & subsequent development. *American Journal of Obstetrics & Gynecology, 180*(1 Pt 1), 114-121.

Golub, M. (1982). Maze exploration in juvenile rats treated with corticosteroids during development. *Pharmacology, Biochemistry & Behavior, 17*(3), 473-479.

Hediger, M. L., et al. (2002). Birthweight and gestational age effects on motor and social

development. *Paediatric and Perinatal Epidemiology, 16*(1), 33-46.

Huddy, C. L., Johnson, A., & Hope, P. L. (2001). Educational and behavioural problems in babies of 32-35 weeks gestation. *Archives of Disease in Childhood - Fetal Neonatal Edition, 88*, F23-F28.

Kadner, A., et al. (2006). Low-frequency hearing loss in prenatally stressed rats. *Neuroreport, 17*(6), 635-638.

Kumar, P., Seshadri, R., & Grobman, W. A. (2004). Neurodevelopmental outcome of very low birth weight infants after multiple courses of antenatal corticosteroids. *Journal of the Society for Gynecologic Investigation, 11*(7), 483-487.

Low, J. A., et al. (1992). Association of intrauterine fetal growth retardation and learning deficits at 9 to 11 years of age. *American Journal of Obstetrics & Gynecology, 167*, 1499-1505.

Matthews, S. G. (2000). Antenatal glucocorticoids and programming of the developing CNS. *Pediatric Research, 47*(3), 291-300.

NIH Consensus Development Conference. (1994). *Report of the consensus development conference on the effect of corticosteroids for fetal maturation on perinatal outcome.* Bethesda MD.

NIH Consensus Development Conference. (2000). *Antenatal corticosteroids: Repeat courses. NIH Consensus Statement.* Bethesda MD.

O'Shea, T. M., et al. (2007). Follow-up of a randomized, placebo-controlled trial of dexamethasone to decrease the duration of ventilator dependency in very low birth weight infants: Neurodevelopmental outcomes at 4 to 11 years of age. *Pediatrics, 120*(3), 594-602.

Parikh, N. A., et al. (2007). Postnatal dexamethasone therapy and cerebral tissue volumes in extremely low birth weight infants. *Pediatrics, 119*(2), 265-272.

Stromswold, K. (2002). *The Parent Assessment of Language (PAL) Test*.

Stromswold, K. (2006a). *The Parent Assessment of Language (PAL) Test - Revised*.

Stromswold, K. (2006b). The validity of the Parent Assessment of Language (PAL) test for preschool-aged children. *Rutgers University Center for Cognitive Science (RuCCS) Technical Report, 83*.

Stromswold, K. (2006c). Why aren't identical twins linguistically identical? Genetic, prenatal and postnatal factors. *Cognition, 101*, 333-384.

Stromswold, K., et al. (2006). Parents can test preschool children's language: The Parent-Assessment of Language (PAL) test. *RuCCS Technical Report, 84*.

Taylor, H. G., Klein, N. K., & Hack, M. (2000). School-age consequences of birth weight less than 750 g: A review & update. *Developmental Neuropsychology, 17*, 289-321.

Taylor, H. G., et al. (2000). Verbal memory deficits in children with less than 750 g birth weight. *Child Neuropsychology, 6*(1), 49-63.

Uno, H., et al. (1994). Neurotoxicity of glucocorticoids in the primate brain. *Hormones & Behavior, 28*(4), 336-348.

Walther, F. J. (1988). Growth and development of term disproportionate small-for-gestational age infants at the age of 7 years. *Early Human Development, 18*, 1-11.

Wapner, R. J., et al. (2007). Long-term outcomes after repeat doses of antenatal corticosteroids. *New England Journal of Medicine, 357*(12), 1190-1198.

Wiig, E. H., Secord, W., & Semel, E. (1992). *Clinical Evaluation of Language Fundamentals – Preschool*. San Antonio, TX: The Psychological Corporation.

Wiig, E. H., Secord, W. A., & Semel, E. (2004). *Clinical Evaluation of Language Fundamentals - Preschool, Second Edition*. San Antonio, TX: Harcourt Assessment.