

**HYPNOTIZABILITY  
AND  
CORPUS CALLOSUM MORPHOLOGY**

By

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# Hypnotizability and Corpus Callosum Morphology

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(Abstract)

In general, highly hypnotizable individuals (“highs”) have exhibited greater abilities to focus attention and inhibit pain than low hypnotizable individuals (“lows”). Furthermore, highs appear to have faster neural processing than lows. The present study investigated differences between lows and highs in morphological volume of some brain structures associated with inhibitory and excitatory neural processing, particularly the corpus callosum (CC).

Participants were 18 healthy university students, aged 18 to 29, with no history of concussion or medical disorders. They were in a functional Magnetic Resonance Image (fMRI) study examining the neurophysiology of pain and hypnotic analgesia (Crawford, Horton, Harrington, et al., 1998; Downs et al., 1998). As assessed by the group version (Crawford & Allen, 1982) of the Stanford Hypnotic Susceptibility Scale, Form C (SHSS:C; Weitzenhoffer & Hilgard, 1962), there were eight highs (four women and four men; SHSS:C M = 11.0) and 10 lows (five men and five women; SHSS:C M = 2.1). Highs were able to successfully eliminate perception of pain and distress to experimental noxious stimuli. Their anatomical MRIs were measured to assess relationships between brain structure volume (CC, medial cortex, anterior brain regions) and hypnotizability. In comparison to lows, highs had a significantly larger CC volume in the rostrum and isthmus, inferred to reflect larger transcallosal axon diameter or greater axon myelination. For highs, but not lows, there were significant relationships between forebrain volume and the total CC, rostrum, and splenium. Findings provide support for the neuropsychophysiological model of Crawford and her associates (e.g. Crawford, 1994a, 1994b; Crawford & Gruzelier, 1992) proposing a more effective attentional system of inhibitory processes in highs than lows. Furthermore, the data suggest that the more effective systems of attentional and inhibitory processes enhanced

neural processing speed, and interhemispheric transfer times seen in highs than lows, may be associated with morphological differences in certain anterior and posterior CC regions. These regions are known to be involved in the allocation of inhibitory and excitatory transfer of information between hemispheres.

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# CHAPTER 1

## INTRODUCTION

### Overview

Hypnosis is a highly effective behavioral intervention in the relief of acute and chronic pain among hypnotically responsive individuals but not hypnotically unresponsive individuals (e.g., Barber, 1996; E. R. Hilgard & J. R. Hilgard, 1983, 1994; J. R. Hilgard & LeBaron, 1984). Highly hypnotizable individuals appear to possess greater abilities to partition attentional resources that inhibit unwanted stimuli from reaching perceptual awareness (for reviews, see Crawford, 1994a, 1994b, in press; Crawford & Gruzelier, 1992; Crawford, Knebel, & Vendemia, 1998; E. R. Hilgard, 1986; E. R. Hilgard & J. R. Hilgard, 1994). Prior research suggests that hypnotic analgesia involves an active process of supervisory, executive control by the anterior frontal cortex (Crawford, 1990a; Crawford, Gur, Skolnick, Gur, & Benson, 1993; Crawford, Horton, Harrington, et al., 1998; Crawford, Knebel, & Vendemia, 1998; Kropotov, Crawford, & Polyakov, 1997). Since the anterior frontal cortex interacts with and modulates other parts of the brain by activating or inhibiting particular schemata (Frith, 1991), it is proposed that there may be underlying brain morphological differences between those who can and cannot eliminate all perception of pain and distress accompanying experimental pain.

Structural neuroimaging studies have suggested that there are associations between volumetric size of brain structures and cognitive processing differences in populations with and without psychopathology (e.g., Corballis, Boyd, Schulze & Rutherford, 1998; Davatzikos & Resnick, 1998; Marsh et al., 1999; Matano, & Nakano, 1998; Robichon & Habib, 1998; Tibbo, Nopoulos, Arndt & Andreasen, 1998; Wassink, Andreasen, Nopoulos, & Flaum, 1999). The corpus callosum (CC) has been the subject of many of these analyses and may be especially salient for consideration based upon its proposed role in attention and allocation of inhibitory and excitatory transfer of information between hemispheres of different brain regions.

Several imaging techniques and paradigms are currently used to identify the dynamic activity of neural functioning and brain systems. Positron Emission Tomography (PET),

Magnetic Resonance Imaging (MRI), and electrophysiological studies have revealed a widespread neuronal network of brain systems working both sequentially and in parallel. The method of brain imaging producing the best spatial resolution and localization at this time is MRI or functional magnetic resonance imaging (fMRI). However, only a few researchers are using MRI and fMRI technology to investigate correlations between neurophysiological differences and behavioral or cognitive traits.

In our ongoing research that uses fMRI to investigate neural pathways of pain and the inhibition of pain perception in low and highly hypnotizable individuals, we identified activation pattern differences between low and highly hypnotizable individuals, particularly during hypnotic analgesia (Crawford, Horton, Harrington et al., 1998; Downs et al., 1998). Prior neurophysiological differences in EEG and event related potentials (ERP) between low and highly hypnotizable individuals have been observed and related to attentional differences (for review, see Crawford, 1994a, 1994b; Crawford, Knebel, & Vendemia, 1998; Crawford, Knebel, Vendemia, & Horton, in press; Crawford & Gruzelier, 1992).

Hypnotic susceptibility is a cognitive trait that correlates with sustained and focused attentional abilities (Crawford, Brown & Moon, 1993; Tellegen & Atkinson, 1973). It is also associated with differences in brain dynamics in waking and hypnosis conditions as assessed by electrophysiological (Crawford, 1994a, 1994b; Crawford, Knebel, & Vendemia, 1998; Crawford, Knebel, Vendemia, & Horton, in press; Crawford & Gruzelier, 1992), regional cerebral blood flow (Crawford, Gur, et al., 1993), positron emission tomography (Rainville, Duncan, Price, Carrier, & Bushnell, 1997; Rainville et al., 1999; Wik, Fischer, Bragee, Finer, & Fredrikson, in press) and fMRI (Crawford, Horton, Harrington et al., 1998; Downs et al., 1998) studies.

This study is concerned with the differential ability of low and highly hypnotizable individuals to eliminate pain during hypnotic analgesia and extends this work to assess whether there are underlying morphological differences related to the ability to control pain perception. This study is based on theoretical models of inhibitory CC functioning (e.g., Cook, 1986; Chiarello, 1995) and the gating hypothesis of Banich (1995a, 1995b). It is hypothesized that the more effective transfer of inhibitory information via the anterior CC is correlated with larger diameter or more myelination of the axons involved in interhemispheric

information integration. Furthermore, larger diameter or more myelinated axons would result in a larger volume of brain structure that is morphologically different. The more effective transfer of inhibitory information via the CC may relate to the ability of highly hypnotizable individuals to inhibit the perception of pain and be indicated by significantly different anterior CC volume in low and highly hypnotizable individuals.

A pilot study for this study was completed using the anatomical MRIs of the ten low and eight highly hypnotizable participants of the ongoing fMRI pain study. The pilot study involved measurements of the CC using a single midsagittal image of each of the participant's anatomical MRI.

The image was selected and the CC was divided into seven sections by the straight-line method developed by Witelson (1989). The straight-line method of division is geometrically based and divides the CC into anterior and posterior halves. It further divides the CC into anterior and posterior thirds that separates the anterior mid-body from the rostral body and separates the posterior mid-body from the isthmus. The division further separates the genu and rostrum from the rostral body by a vertical line drawn through the most posterior portion of the curve of the genu. A vertical line delineating the posterior 20% of the CC separated the splenium from the isthmus. The total area of the CC and each of the seven areas were measured using the Scion Image (Scion Corporation) program. The pilot study revealed a significant size difference with the anterior region of the CC being larger in the highly hypnotizable individuals ( $p < .001$ ).

It should be noted that there were several issues not addressed in the pilot study that were addressed in this study.

1. The pilot study only addressed the anterior region of the CC.
2. The pilot study used a single midsagittal slice of the MRI to determine CC size.
3. The method of CC division used in the pilot study was based on the straight-line method of Witelson (1989) and did not consider the curvature of the CC.
4. The pilot study did not include procedures to reorient the images to align the anterior commissure and posterior commissure to a common horizontal reference.
5. The pilot study did not include any brain structures other than the CC.

This study evaluated all regions of the CC, used new methodological approaches and

included procedures to better control the consistency of measurements across participants. In addition to the evaluation of the CC, this study also evaluated other brain regions, including the frontal area of the brain, the overall medial cortex, and the anterior cingulate to determine if there were further hypothesized relationships to hypnotizability. Finally, it assessed hypothesized relationships between CC size and forebrain size.

## CHAPTER 2

### REVIEW OF THE LITERATURE

This chapter reviews selected literature pertaining to brain structure, behavioral, physiological and hypnosis research. The literature relates current knowledge and theoretical models to questions addressed in this study.

#### Corpus Callosum Research

Even though it is apparent that the commissures of the brain, including the CC, in some way integrate the activity of the separate hemispheres, the exact function of the CC remained a mystery until the first research involving commissurotomy in epileptic patients. In 1940, “Warren McCulloch concluded . . . that the only certain role of the corpus callosum was ‘to aid in the transmission of epileptic seizures from one to the other side of the body’” (Kupfermann, 1991, pp. 833). It has also been reported that Karl Lashley made the facetious statement around 1950 that “the purpose of the corpus callosum ‘must be mainly mechanical . . . to keep the hemispheres from sagging’” (Kupfermann, 1991, pp. 833). Prior to the 1950s the function of the CC was not well understood, and the CC was considered to serve only as a bridge between the hemispheres without any other known functional involvement. This view has slowly evolved to an acknowledgement of its active involvement in the excitatory and/or inhibitory transfer and integration of information between hemispheres.

The importance of the CC and its role in interhemispheric communication began with the "split brain" research of epileptics by Michael Gazzaniga and Roger Sperry in the 1960s. However, this research was limited to behavioral observations of individuals who had their CC severed (Gazzaniga, 1997). Beginning in the 1980s, research was extended to an investigation of the relationship of CC morphology to sex, handedness, age, and behavior (e.g., Clarke, Kraftsik, Van der Loos, & Innocenti, 1989; Witelson, 1985, 1989; Witelson & Goldsmith, 1991).

Now researchers agree the human brain has two anatomically distinct, but functionally complementary (Gazzaniga, 1997), cerebral hemispheres involved in processing information

that is transferred bilaterally by only a few major commissure tracts including the anterior commissure (AC), the posterior commissure (PC), the hippocampal commissure, the thalamic bridge, and the CC. The CC is the primary commissure through which interhemispheric communication occurs. The composition of the CC includes the myelinated axons of over 200 million neurons (Jäncke & Steinmetz, 1997). The axons in the CC are of varying diameters and serve to connect homotopic regions of the opposing hemispheres of the brain and integrate information from both hemispheres.

### Corpus Callosum Divisions

The homotopic areas of cortex connected by the CC are typically associated with general regions of division of the CC. Most CC morphological studies have employed one of two common methods of division: the radial method of Clarke et al. (1989) as shown in Figure 2.1 and the straight-line method of Witelson (1989) as shown in Figure 2.2. The radial method of division used by Clarke et al. (1989) used a curved reference line that took into consideration the curvature of the CC. The radial division method requires one to first transfer the center of gravity of the CC to a baseline located at the most inferior part of the anterior and posterior portion of the CC. The CC is then divided into approximate halves and a total of six sections by use of 90 degree, 60 degree and 30 degree lines that originate at the transferred center of gravity at the baseline and extend to intersect the CC. Witelson's (1989) straight-line method is geometrically proportional and divides the human CC into a topography of cortical origin and termination of callosal fibers that is based upon and roughly approximates the topography determined in non-human primates. She proposed seven major areas that project to and connect homotopic cortical regions; these approximate the division of functional cortical regions of the non-human primate CC. As illustrated in Figure 2.2, Witelson's straight-line method of division geometrically proportions the CC into the rostrum and genu, the anterior third, the anterior half, the posterior half, the posterior third and the splenium as the posterior fifth of the CC.

The areas of projection of the CC fibers are based on non-human primate studies and correspond approximately to Witelson's (1989) geometric divisions. Table 2.1 summarizes

the geometric divisions with the common name and area number referred to in the general literature and their approximate topographic projections.

Witelson's (1989) divisions, as illustrated in Figure 2.2, were based upon non-human primate studies but employ geometric intervals for division of the CC. Other researchers have used different divisions in an attempt to better control the consistency with which the CC is functionally divided in humans (e.g., Clarke et al., 1989; Habib et al., 1991; Nasrallah et al., 1986; Tan et al., 1991). Unterrainer et al. (1997) graphically compared the seven divisions of Witelson (1989) to that of the schematic topography of the non-human primate labeling studies. Their comparison suggests that the geometric basis of division of the human CC may not accurately reflect the cortical topography represented by the callosal fibers. In humans and non-human primates, the splenium topography is very similar with the division based on the posterior 20% of the CC. The posterior portion of the Splenium contains visual area fibers and the anterior portion of the Splenium contains fibers connecting homotopic areas of the inferior temporal area. The superior temporal area of the brain is connected by fibers in the posterior portion of the isthmus. The anterior portion of the isthmus, the posterior mid-body and the posterior portion of the anterior mid-body of the CC is topographically represented in non-human primate labeling studies as one area connecting homotopic areas of the posterior parietal area. The anterior portion of the anterior mid-body in humans is comparable to a small area of the non-human primate CC that connects the homotopic areas of sensory areas of the brain. The portion of the non-human primate CC that connects the motor areas of the brain is comparable to the posterior portion of the rostral body combined with the ventral portion of the anterior part of the rostral body in the human CC. The anterior and superior portion of the rostral body in humans may be compared to the area of non-human primate CC that homotopically connects the premotor area of cortex.

The non-human primate functional map and Witelson's division of the human CC differs in the projection of the superior portion of the rostral body. The more anterior projection of the superior portion of the CC rostral body of the non-human primate projects into the analogous area of the genu and contains premotor fibers instead of anterior frontal fibers. The genu of the non-human primate CC contains fibers connecting the anterior frontal area of cortex (approximately analogous to BA 9 of the human cortex) and is similar to the division

for the genu represented by Witelson's divisions. The inferior portion of the genu in the non-human primate CC is not as pronounced as it is in the human CC and the non-human primate rostrum is more anterior in the inferior portion of the genu.

Both Witelson's (1989) and Clarke et al.'s (1989) divisions are geometrically based and only approximate the already well identified functional divisions of the cortex to which the callosal fibers are projecting. Therefore, it may be advantageous to use a different method of division yielding smaller CC regions for the purpose of area analyses to ensure more accurate comparison to functional cortical areas of interest. When Aboitz, Scheibel, Fisher, and Zaidel (1992) sampled CC tissue for the purpose of measuring differences in axon diameter in different areas of the CC, they used the standard divisions of Witelson (1989) but sampled from three evenly spaced regions within each geometric division.

Research regarding fiber distribution (Aboitz, Scheibel, Fisher, & Zaidel, 1992) and functional projections (Tan et al., 1991) suggest a smaller division of the CC. Dividing the CC into smaller 1 cm sections, or twelve approximately equal lengths (Tan et al., 1991), could facilitate more detailed comparison of relationships of CC volume with cognitive and functional differences of attentional and inhibitory capabilities. However, in order to have a more direct comparison to past research, this study used the more standard divisions of anterior and posterior fifths, thirds and halves in the manner of Clark et al. (1989), as illustrated in Figure 2.1. Additionally, the rostrum was separated in the manner of Witelson (1989), as illustrated in Figure 2.2.

Morphological research has used several methods to investigate the morphology of brain structures. The two most common techniques of investigating morphology and size of the CC have been the measurement evaluation of postmortem brain or living brain structure by the use of MR imaging. Research has addressed correlations of CC structure to handedness, sex and cognitive functioning in populations with and without psychopathology. Selected literature and studies involving these two major approaches are reviewed in the next sections.

### Postmortem Studies of the Corpus Callosum

The CC is a large, easily identified, and relatively easily quantifiable structure of the

brain. Because it is so large and easily quantified, it was one of the first brain structures to be measured and studied quantitatively (Leonard, 1997). Since postmortem studies must rely on identifiable differences, they are traditionally limited to analyses of variables such as handedness and sexual dimorphism.

The results of postmortem studies investigating CC size and handedness are relatively consistent, but studies of sexual dimorphism are rather inconsistent. Non-consistent right-handed individuals have larger CCs than consistently right-handed individuals (Witelson, 1985, 1989; Witelson & Goldsmith, 1991). Investigations of the effects of sexual dimorphism on CC size yielded mixed findings including a larger and more bulbous splenium in women (de Lacoste-Utmasing & Holloway, 1982), a larger total size of the CC in women (Holloway & de Lacoste, 1986), a general overall increased CC size in men (Clarke et al., 1989), and an interaction between handedness and sex with a larger genu in men (Witelson, 1989). By contrast, Going and Dixson (1990) found no sex differences in actual or proportionally corrected size comparisons. Yet, Matano and Nakano (1998) found larger overall cortex and CC dimensions in men that disappeared when corrected for proportional size. Ringo, Doty, Demeter, and Simard (1994) proposed that smaller volume brains, whether male or female, had larger corpora callosa because the CC had more room to develop larger diameter axons since there was less cortical mass occupying the available space in the cranial cavity.

As researchers became more interested in the anatomical structure of the CC, they evolved towards including an evaluation of the fiber composition of the neurons of the CC as well as topographical mapping studies. These studies included analyses of fiber composition and distribution of the CC (Aboitz, Scheibel, Fisher, & Zaidel, 1992), morphometry of the CC (Aboitz, Scheibel, & Zaidel, 1992), and topographic distribution of the callosal fibers (Meyer, Roricht, & Woiciechowsky, 1998).

Fiber composition and distribution studies revealed that higher order processing areas of the cortex, such as the frontal areas (e.g., Brodmann areas 8, 9 & 10) involved in attention project to the CC through axons as small as 0.4 micrometers in diameter in the genu and rostrum of the CC (Aboitz, Scheibel, Fisher, & Zaidel, 1992). Axons as large as 3 to 5 micrometers in diameter are more prevalent in the posterior mid-body of the CC. The greatest densities of large diameter axons are located in the posterior mid-body with the smaller

diameter fibers being more concentrated in the anterior and far posterior regions of the CC.

Since MRI technology is not yet sufficient to yield the resolution required for fiber studies, only postmortem studies can reveal direct information about fiber quantities, diameters or amount of myelination. The measurement of area or volume of different sections of the CC is an indirect measure indicative of differences in axon diameter, myelination or quantity in any given section. The indirect measure of area or volume of brain structures, including the CC, has been used to assess relationships with various disorders involving attention and/or inhibitory deficits. Investigations of obsessive-compulsive disorder (e.g., Robinson et al., 1995; Jenike et al., 1996) and attention deficit hyperactivity disorder (ADHD) (Filipek et al., 1997; Mataro, Garcia-Sanchez, Junque, Estevez-Gonzalez, & Pujol, 1997) found decreased area or volume of certain brain structures. It logically follows that indirect measures of area or volume may be correlated with efficiency of processing for somatosensory stimuli in the posterior mid-body, motor ability in the anterior mid-body, attentional processes in the anterior sections of the CC and visuospatial abilities in the posterior sections of the CC.

Postmortem studies that are concerned with mapping and tracing topographical distribution (e.g., Aboitz, Scheibel, Fisher, & Zaidel, 1992; Aboitz, Scheibel, & Zaidel, 1992; Meyer, et al., 1998) typically do not account for dimension change of the postmortem brain. However, postmortem studies involving measurement of brain structures such as the CC (e.g., Jäncke & Steinmetz, 1997; Witelson, 1985, 1989; Witelson & Goldsmith, 1991) must consider the dimension change of the postmortem brain. Measurements of the postmortem brain need to be adjusted to account for as much as a 9% increase in brain volume due to absorption of cerebral spinal fluid that occurs during the first few hours after death (Jäncke & Steinmetz, 1997). MRI studies do not have to contend with the problem of absorption of cerebral spinal fluid since the images are from living participants. However, “volume adjustment”, as recognized in MRI studies, is a compensation used in MRI measurements that involves a process referred to as partial volume averaging whereby the voxels on the edge of a structure will contain elements of adjacent structures and therefore have an “average” intensity. This reduces the accuracy of overall volume measurements from MRI images (Personal communication, J. Hunter Downs, III, March 19, 1999).

## MRI Studies of the Corpus Callosum

MRI technology produces an image, as illustrated in Figure 3, that is easily measured and facilitates analyses of brain structure morphology by providing researchers with a method for the noninvasive acquisition of brain images from living participants. The relative ease of image acquisition has encouraged researchers to use MRI technology to continue to investigate handedness and sexual dimorphism and has allowed researchers to extend studies to brain structure morphology of living pathological and normal individuals. The relationships of the CC to other brain structures and to pathologies such as schizophrenia, obsessive-compulsive disorder, attention deficit disorder, and dyslexia have been investigated. MRI studies are now directing attention to anatomical correlates of cognitive and perceptual processing in healthy individuals.

MRI research assessing the relationship between CC volume and handedness and sex continues to have mixed results. Some researchers have reported no sex differences relative to the size of the CC (Byne, Bleir, & Houston, 1988; Hopper, Patel, Cann, Wilcox, & Schaeffer, 1994), whereas others have reported a decrease in the overall size of the CC correlated with age but not sex (Hopper et al., 1994). Habib et al. (1991) confirmed Witelson's (1985) postmortem findings of sex and handedness interactions with larger corpora callosa in non-consistent right-handed women. Davatzikos and Resnick (1998) reported larger CCs and greater bulbosity, as defined in Figure 2.1, correlated with better cognitive performance in women; yet this relationship was not observed in age-matched men. In a more pathological investigation of individuals with gender dysphoria, Emory, Williams, Cole, Amparo, and Meyer (1991) found no significant differences between transsexuals of either genetic sex or the controls.

MRI techniques have been used to investigate cognitive and attentional process by volume analyses of different brain structures, particularly the CC, in various pathologies. In comparison to controls, patients diagnosed with schizophrenia were found to have significantly smaller brain structures: basal ganglia (Hokama et al., 1995), white and gray matter (Marsh et al., 1999), cerebellar size (Wassink, et al., 1999), and CCs (Tibbo et al.,

1998). The possible effects of prior medications have not been well evaluated.

In general, MRI studies have shown that individuals with attention and/or inhibitory deficits had smaller corpora callosa, particularly in the anterior region. Patients with obsessive compulsive disorder had less volume of the caudate nucleus (Robinson et al., 1995) and a reduction in the amount of total white matter including the CC (Jenike, et al., 1996). Individuals with ADHD had a smaller caudate nucleus and overall reduced white matter (Filipek et al., 1997; Mataro et al., 1997) with a particularly significant decrease of the rostral body of the CC (Baumgardner et al., 1996). This study proposed that low hypnotizables, known to have greater distractibility and less effective sustained attentional processing, would have significantly smaller anterior portions of the CC than highly hypnotizable individuals. This hypothesis is expanded upon in a later section.

### Theories of Corpus Callosum Functioning

Historically, there are at least two different approaches or models that have addressed corpora callosa functioning. One such model proposes excitation, neural synchronicity and laterality effects (e. g. Engel, König, Kreiter, & Singer, 1991; Gazzinga, 1997; Gazzinga & Sperry, 1967; Singer, 1995). It suggests that the CC serves an excitatory function that results in homotopic interhemispheric excitation, or transfer of the same information from a specific area of one hemisphere to the same area of the other hemisphere. Homotopic interhemispheric excitation results in duplicity of information in the hemispheres (for reviews, see Berlucchi, 1983; Clarke & Zaidel, 1994). By contrast, a more widely accepted model of CC functioning proposes inhibition and laterality effects (Cook, 1986). It suggests that the CC maintains independent processing of the hemispheres by inhibiting the transfer of information homotopically and thereby allowing one hemisphere to operate without influence on the other hemisphere. The fibers involved in the transmission of the neural impulses through the CC are excitatory in nature, but inhibition may occur at inhibitory post callosal interneurons. Thus, the inhibitory model of laterality predicts that laterality and hemispheric specialization should be positively related to the amount of interhemispheric connectivity and conduction, while the excitatory model of laterality predicts that there would be an inverse

relationship between laterality and connectivity. There are a number of recent reviews of research involving interhemispheric transfer of information and CC functioning (Banich, 1995a, 1995b; Chiarello, 1995; Hellige, 1995; Robertson, 1995; Sergent, 1995; Zaidel, Aboitz, Clarke, Kaiser & Matteson, 1995). A third model proposes that the CC is involved in both excitatory and inhibitory processing (e.g. Banich, 1995a, 1995b, 1998; Chiarello, 1995).

Other theories of CC functioning theories are based on the main models of excitation and laterality or that of inhibition. Ringo et al. (1994) proposed a theoretical model based on excitation with CC function involving interhemispheric transfer time (IHTT) and hemispheric specialization. IHTT is the time required for an action potential to travel from one hemisphere to the other via a commissure such as the CC. Ringo et al. (1994) determined approximate IHTT by calculating the transcallosal conduction distances, based on non-human primate studies, and transcallosal conduction time, based on average fiber diameters, that were transformed into conduction velocities. They assumed a linear proportionality for conduction velocity of myelinated fibers to axon diameter (without the myelin) and a proportionality constant of 8.7 mm/msec/ $\mu$ m of axon diameter. The formula for calculation of conduction velocity for an axon of any given diameter then is as follows: conduction delay (msec) = distance (mm)  $\div$  [diameter ( $\mu$ m)  $\cdot$  8.7 (mm/msec/ $\mu$ m)]. Thus, by dividing the conduction distance by conduction velocity, they projected the time required for an action potential to cross the CC for axons of any particular diameter.

In their theoretical model of IHTT, Ringo et al. (1994) proposed that smaller brains have larger corpora callosa because smaller brains occupy less cranial space and consequently have more physical space for the development of larger diameter axons in the CC. The larger diameter axons in the CC allow for more effective interhemispheric conduction and therefore faster IHTT. They further proposed that larger brains occupy more cranial space and, therefore, have less physical space for the development of larger diameter axons in the CC and subsequently result in smaller corpora callosa due to the axons having an overall smaller diameter. If so, then a larger brain would have limited axonal development and a smaller corpus callosum would result in longer transcallosal conduction delay and consequently less effective interhemispheric transfer. The less effective interhemispheric transfer would then influence the development of more lateralized processing of information or hemispheric

specialization due to the increasing time constraints of transcallosal conduction delay that accompanies increasing brain volume.

Banich (1995b) proposed a working model of interhemispheric processing that emphasized a different approach to laterality research. She proposed that “interhemispheric processing can increase the processing capacity of the brain by allowing for a dispersal of processing load across the hemispheres, and that such a dispersal is especially useful when tasks are difficult” (p. 440). Her intriguing concept conceives the CC to act like a “gate” that allows information to cross hemispheres and engage in simultaneous parallel processing only when the predominant hemisphere has reached its capacity. Thus, her model proposes both excitatory and inhibitory processes occurring in the CC. She additionally argued that deficits in interhemispheric processing are present in a “surprisingly large variety of syndromes, including alexithymia, pedophilia, dyslexia, schizophrenia, multiple sclerosis, and attention-deficit disorder” (p. 444) all of which can be explained by a lack of inhibitory processing that involves the CC. More recently, Banich (1998) expanded her view for the role of the CC in “gating” information between hemispheres. She proposed the CC to be involved in not only transferring sensory information between hemispheres but also for the important role of integrating attentional processing. Her argument for deficits in attentional processes and interhemispheric processing are supported by morphological studies of pathologies such as ADHD (Baumgardner et al., 1996; Filipek, et al., 1997; Mataro et al., 1997) and dyslexia (Robichon & Habib, 1998; Rumsey et al., 1996) that found significant differences in size and morphology of the CC. In a subsequent section, it is proposed that low hypnotizables may also show deficits in interhemispheric processing.

The literature regarding CC functioning was richly enhanced by Liederman (1995) when she examined the traditional view of the disconnection syndrome in split-brain patients, rejected it and proposed an alternate approach. She proposed that there is (1) a direct transfer of explicit information that occurs through cortical connections (primarily the CC that is severed in the split-brain) and (2) an indirect or subcortical transfer of implicit information. Drawing upon experimental support, she contended that subcortical pathways are able to integrate categorical or context dependent, fragmented information which can be accessed only implicitly.

An additional conceptualization of CC functioning has been proposed by Chiarello (1995) who argued that when one hemisphere is activated by an ambiguous prime, the CC acts to inhibit duplicate information and subsequently produces complementary information in the opposing hemisphere. Chiarello's experimental results tend to support the theory of CC excitation and duplication more than her conceptualization of duplicate inhibition and production of complementary information.

In summary, this field is in a state of flux as new data support or refute specific theoretical models. Yet, the more recent models proposing functional duality of excitatory and inhibitory CC processes (e.g., Banich, 1995a, 1995b, 1998; Chiarello, 1995) are the models that are more supported by recent behavioral research reviewed below.

### Behavioral Studies in Corpus Callosum Research

Since Ringo et al. (1994) introduced the concept of IHTT and conduction velocity being dependent on conduction volume and the diameter of the axons in a commissure, behavioral CC studies have been interested in the efficiency of interhemispheric transfer of information and attentional processes. Jäncke, Staiger, Schlaug, Huang, and Steinmetz (1997) investigated the relationships of handedness and sex to the morphology of the CC. They found no handedness or sex effects but did find that an increased CC size (total CC, anterior third, and isthmus of the CC) correlated with an increased forebrain volume. They interpreted these data as being suggestive of a relationship between CC efficiency and attentional processes.

With interest increasing in CC functioning and attention, Rueckert and Levy (1996) investigated CC efficiency indirectly through studies of sustained attention and IHTT. They investigated the efficiency of information integration between hemispheres in the frontal lobes of the brain via the anterior regions of the CC. Participants were first tested on a vigilance task with a varied interstimulus interval and then they were required to perform incongruent tasks with their left and right hands simultaneously. Participants who exhibited less interference between the two hands during the simultaneous incongruent tasks also missed fewer signals on the vigilance task after the longer interstimulus intervals. It was concluded

that better interhemispheric integration of information via the CC resulted in enhanced parallel processing and, thus, less interference between hands during an incongruent task. Furthermore, the individuals who exhibited less interference between the two hands also missed fewer signals on a vigilance task that indicated more effective sustained attention abilities. Thus, Rueckert and Levy (1996) concluded that the CC is involved in the ability to sustain attention over a long period.

Larson and Brown (1997) examined IHTT and hemispheric specialization by presenting differing stimuli to one or both visual fields and measuring the difference in the resulting crossed or uncrossed activation times of an event related potential (ERP). The differing stimuli consisted of matched (A, A) or unmatched (A, a) letters, presuming left hemisphere dominance for verbal stimuli, and matched or unmatched patterns, presuming right hemisphere dominance for spatial stimuli. They found a significant left visual field advantage for pattern stimuli but did not find any visual field advantage for letters. They also found an overall faster IHTT for right hemisphere to left hemisphere transfer in all situations. They interpreted their findings as suggestive of individual hemisphere dominance being stronger than the traditionally accepted concept of task specific hemisphere dominance. One of the more interesting findings involved a letter-matching task that yielded no correlation of bilateral field advantage with the speed of right to left hemisphere transmission. However, it did yield a negative correlation of bilateral field advantage with the speed of left to right hemisphere transmission (a faster IHTT correlates with a larger advantage for bilateral processing). Larson and Brown (1997) proposed a theory of asymmetric homologue enhancement based on the hypothesis that bilateral processing is enhanced by the transmission speed from the left hemisphere in assisting the right hemisphere due to the less competent verbal processing of the right hemisphere.

The behavioral studies of interhemispheric communication efficiency and IHTT have contributed greatly to our knowledge of CC functioning and efficiency. However, to investigate actual neural processing speed between hemispheres one must measure the IHTT of information from one hemisphere to the other. Crawford's Neurocognition Laboratory is using electrophysiological studies to measure IHTT of low and highly hypnotizable individuals and has shown that in comparison to lows, highly hypnotizable individuals have

faster latencies of certain auditory and somatosensory ERP components as early as 50 msec with some hemispheric differences (Crawford, Horton, & Lamas, 1998; Crawford, Knebel, Xie, et al., under review; Horton, McClain-Furmanski, Mészáros, & Crawford, 1998; Lamas & Crawford, 1998; Lamas, Crawford, & Vendemia, under review; McClain-Furmanski, Horton, & Crawford, 1999). For instance, Crawford, Knebel, Xie, et al. (under review) found somatosensory ERP latency differences that suggest neural processing speed differences across hemispheres in healthy individuals who were low and highly hypnotizable. Highly hypnotizable participants had significantly faster IHTT as determined by differences in ERP component latencies in each hemisphere across several electrode sites in the parietal and frontal areas. These researchers have interpreted their findings as evidence for more effective (faster) neural processing, and possibly IHTT differences, among highly hypnotizable individuals than low hypnotizable individuals.

#### Anterior Cingulate Research

Another brain structure closely associated with executive functioning that mediates attentional and inhibitory (Posner, 1995; Vogt, Finch, & Olson, 1992) and emotional (Lane et al., 1998) processing is the anterior cingulate. The cingulum is a “C” shaped area of cortex superior to the CC and follows the curvature of the CC extending from the anterior portion of the brain just anterior and inferior to the rostrum of the CC posteriorly to the posterior area of the splenium. The cingulum is divided into the anterior and posterior cingulate with the anterior cingulate being the anterior portion of the cingulum involving Brodmann areas 24, 25, and 32 and is delineated from the posterior cingulate by a sulcus located just superior to the mid-body of the CC. Brodmann areas 24 and 32 are generally considered to comprise the “cognitive” area of the anterior cingulate (Devinsky, Morrell, & Vogt, 1995).

The anterior cingulate has been associated with tasks requiring attentional resources such as those that involve cognitive demands, perceptual demands and response selection (Kolb & Whishaw, 1996). It is known as the executive region of cortex associated with emotion and affect, pain perception, maternal behavior, motor control and attention (for reviews, see Devinsky et al., 1995; Posner, 1995; Vogt et al., 1992). Recent structural neuroanatomical

studies have suggested that there are hemispheric specific associations between the size of the anterior cingulate and attentional and cognitive processing differences in populations with (e.g., Noga, Aylward, Barta, & Pearlson, 1995) and without (e.g., Casey, et al., 1997) known psychopathology. An earlier study by Stanczyk (1987) determined a relationship between cingulate cortex size and frontal lobe development. In a recent neuroimaging study of children without any pathologies, Casey et al. (1997) found significant correlations between a larger anterior cingulate in the right hemisphere and increased attentional performance, but no significant correlations were observed in the left hemisphere.

Even though the cognitive processes, such as attention, are not necessarily concurrent with emotion or affect (Vogt et al., 1992), attention and affect are often combined in pain experiences due to the affective component of pain. Pain studies using PET (Rainville et al., 1997) and fMRI (Crawford, Horton, Harrington et al., 1998; Downs et al., 1998) found a decrease in anterior cingulate activity during hypnotic analgesia in high but not low hypnotizables. Furthermore, Crawford, Gur, et al. (1993) found enhanced anterior frontal activation during hypnotic analgesia among highly hypnotizable participants only; they did not assess anterior cingulate activity. Such differential involvement of the anterior cingulate, as well as the anterior forebrain, during hypnotic analgesia points to possible morphological differences in these regions between low and highly hypnotizable individuals. These possible relationships were investigated in the present study.

### Hypnosis Research

Hypnotic susceptibility is a cognitive trait that correlates with sustained and focused attentional abilities (Crawford Brown & Moon, 1993; Lyons & Crawford, 1997; Tellegen & Atkinson, 1973), inhibitory abilities (e.g., E. R. Hilgard, 1965; Margolis, Domangue, Ehleben, & Shrier, 1983), particularly inhibiting perception of pain (e.g., Crawford, Knebel, Kaplan, et al., 1998; Spiegel, Bierre, & Rootenberg, 1989; Zachariae & Bjerring, 1994; for review, see E. R. Hilgard & J. R. Hilgard, 1994), and differences in brain dynamics (Crawford, 1994a, 1994b; Crawford, Gur, et al., 1993; Crawford, Knebel & Vendemia, 1998; Crawford, Knebel, Vendemia & Horton, in press; Crawford & Gruzelier, 1992; Crawford, Horton, Harrington, et

al., 1998; Gruzelier & Warren, 1993). Hypnosis is a highly effective behavioral intervention for controlling acute and chronic pain primarily due to the ability of highly hypnotizable individuals to partition their attentional resources more effectively and, thereby, eliminate pain perception from conscious awareness (Crawford, 1994a, 1994b; Crawford & Gruzelier, 1992; Crawford, Knebel, Kaplan, et al., 1998; Crawford, Horton, Harrington, et al., 1998; E. R. Hilgard & J. R. Hilgard, 1983, 1994).

There is a robust relationship between hypnotic susceptibility and sustained attention and disattentional abilities (e.g., Crawford, Brown & Moon, 1993; Tellegen & Atkinson, 1973). Hypnotic susceptibility is not only related to sustained attention but also to disattending (ignoring) of extraneous stimuli (Crawford, Brown & Moon, 1993) with highly hypnotizable individuals exhibiting more effective sustained attention and more effective disattentional abilities (Atkinson & Crawford, 1992; Crawford Brown & Moon, 1993). These findings support the premise that highly hypnotizable individuals have more effective “cognitive flexibility” (Crawford, 1989; Crawford & Allen, 1982; Crawford, Clarke, & Kitner-Triolo, 1996) that allows for a better allocation of resources needed for processing information, whether it requires attending or disattending to stimuli (Crawford, 1994a, 1994b). Highly hypnotizable individuals often report more effective sustained attention with higher self-reported absorption (Crawford, Brown, & Moon, 1993; Tellegen & Atkinson, 1973; for a review, see Roche & McConkey, 1990). These findings are often interpreted to support the neuropsychophysiological model proposed by Crawford and Gruzelier (1992) that suggests the involvement of a more effective anterior frontolimbic system (and possibly frontoparietal) in tasks involving sustained attention and requiring the disattention of distractions.

Prior behavioral research shows highly hypnotizable individuals process information faster than low hypnotizables. That it occurs in both non-hypnotic and hypnotic conditions suggests a pervasive trait difference. Highly hypnotizable individuals exhibit faster responses than those low hypnotizable individuals when engaged in complex decision making tasks such as determining an emotion portrayed by faces presented to either the right or left visual fields (Crawford, Kapelis, & Harrison, 1995). They also show faster responses when identifying differences between pictures presented sequentially (Crawford & Allen, 1983) or visuo-spatial stimuli (Mészáros, Crawford, Szabó, Nagy-Kovács, & Révész, 1989).

Recent event-related potential (ERP) research has found that highly hypnotizable individuals have significantly faster ERP component latencies than low hypnotizable individuals. These differences are not affected by condition (waking vs. hypnosis) or strategies (attend vs. ignore instructions). Since shorter latencies reflect faster processing speed, one may infer that highly hypnotizable individuals process information faster at the neurophysiological level. Between 50 and 300 msec post-stimulus, the latencies of somatosensory ERP components to noxious electrical stimuli are typically seen to be significantly faster from anterior frontal to parietal regions among high than low hypnotizables (Crawford, Knebel, Xie, et al., under review; Horton et al, 1998; McClain-Furmanski et al., 1999). Lamas and Crawford (1998) found that highly hypnotizable individuals exhibited faster N200 latencies to standard and deviant tones during an auditory oddball paradigm when asked to attend to and count deviant tones. When individuals were asked to disattend tones and perform a cognitive task, Lamas and Crawford (1998; Lamas, Crawford, and Vendemia, under review) reported that highly hypnotizable individuals had significantly shorter auditory P100 latencies to both standard and deviant stimuli than those low hypnotizable individuals. The shorter P100 latencies occurred in the left anterior, left lateral frontal and medial regions. The N200 latencies to deviant tones were also significantly shorter for highly hypnotizable individuals. Since inhibitory effort requires integrated functional roles of various brain regions, these data agree with the interpretations of Crawford, Knebel, Xie, et al. (under review) that earlier time-locked shifts in the anterior regions of the brain are indicative of excitatory and inhibitory processing involving the active allocation of attention or disattention. Later time locked shifts in the posterior regions were interpreted as indicative of spatiotemporal aspects of somatosensory perceptions. The findings of Crawford, Knebel, Xie, et al. (under review) showed an overall positive going contingent variation in highly hypnotizable participants during hypnotic analgesia that were interpreted as indicative of anticipation of inhibitory control over the regularly occurring stimulus.

Our ongoing fMRI research (Crawford, Horton, Harrington, et al., 1998) showed hemispheric differences in highly hypnotizable individuals during hypnotic analgesia. In comparison to an attend condition, activity was reduced in the supplementary motor area,

insula and anterior cingulate regions in the hemisphere contralateral to the experimental stimulation during hypnotic analgesia. There was also a reduction of activity in the somatosensory association cortex activity suggesting that hypnotic analgesia also impacted the sensory-discriminative system. In a PET study of pain (Rainville et al., 1997; Rainville et al., 1999) similar findings were obtained. Crawford and colleagues (e.g. Crawford 1994a, 1994b; Crawford & Gruzelier, 1992; Crawford, Horton, Harrington, et al., 1998) concluded that the difference in the neurophysiological activity of highly hypnotizable individuals during hypnotic analgesia resulted from more effective inhibitory abilities. Since there was bilateral activation of the anterior frontal cortex during hypnotic analgesia, they further concluded that the highly hypnotizable individual's ability to inhibit pain required inhibitory effort that involved the anterior frontal cortex.

### Hypnosis and Electroencephalographic Changes

A robust finding in the literature is that highly hypnotizable individuals generate more theta (3-7 Hz) EEG activity in waking condition, and even more so during hypnosis, than low hypnotizable individuals (for a review, see Crawford, 1994a, 1994b). Increased theta activity in highly hypnotizable individuals has been reported during rest (Graffin, Ray, & Lundy, 1995; Sabourin, Cutcomb, Crawford, & Pribram, 1990), hypnotic suggestions (Sabourin et al., 1990), experiences of pain (Crawford, 1990b), and positive and negative emotional states (Crawford et al., 1996). Since increased theta has been associated with cognitive effort and sustained attentional tasks (Klimesch, 1995; Schacter, 1977), increased theta activity among highly hypnotizable individuals is interpreted as reflecting their more effective abilities for focused attention or disattention.

There are reported findings of enhanced theta power in highly hypnotizable individuals in both hemispheres (Graffin, Ray, & Lundy, 1995; Sabourin et al., 1990) or in one hemisphere relative to the other (Crawford et al., 1996). Sabourin et al. (1990) found increased theta power among highly hypnotizable individuals at the frontal (F3, F4), central (C3, C4) and occipital (O1, O2) regions during conditions of waking rest and even more so during hypnotic rest and suggestions. Graffin et al. (1995) found it more localized to the

frontal region. More germane to the present study, Crawford (1990b) found highly hypnotizable participants generated significantly more high theta activity than did low hypnotizables at frontal to occipital regions during attend and hypnotic analgesia conditions to cold pressor pain.

In a study of positive and negative emotional states, Crawford et al. (1996) found that highly hypnotizable individuals did not differ from low hypnotizable individuals in the low range of alpha or theta activity. However, during self-generated happy and sad emotions, “highs showed significantly greater hemispheric asymmetries (right greater than left) in the parietal region in high theta (5.5 – 7.45 Hz), high alpha (11.5 – 13.45 Hz), and beta activity between 16.5 and 25 Hz – all frequency bands that are associated with sustained attentional processing” (p. 239). Those low hypnotizable individuals showed no significant hemispheric differences. Based upon Heller’s (1993) model, the greater right parietal activation may reflect greater involvement in emotional states among highly hypnotizable individuals than low hypnotizable individuals.

The higher Hz range of theta (5.5-7.5 Hz) activity is proposed to be associated with preparation for attentional and inhibitory activity that may involve the hippocampal and frontal attentional system (e.g., Crawford, 1994a, 1994b; Crawford & Gruzelier, 1992; Schacter, 1977). If higher theta activity is associated with attentional and inhibitory preparation and response processes, one may interpret the increased amount of higher theta activity observed in highly hypnotizable individuals to be reflective of underlying neurophysiological functioning correlated with their abilities to more effectively attend or disattend to stimuli.

Greater EEG asymmetries and shifts in hemispheric dominance have been observed in highly hypnotizable individuals in several studies that used different paradigms. MacLeod-Morgan and Lack (1982; see also De Pascalis & Palumbo, 1986) reported asymmetries in EEG activity, referred to as “hemispheric specificity”, in highly hypnotizable individuals but not in low hypnotizable individuals while performing tasks during waking and during hypnosis. Subsequent studies reported greater asymmetries in EEG activity among highly hypnotizable individuals during rest and hypnotic suggestions (Sabourin et al., 1990), self-generated emotional states (Crawford, et al., 1996) and painful stimulation (Crawford, 1990b;

DePascalis & Perrone, 1996).

In response to cold pressor pain, Karlin, Morgan and Goldstein (1980) reported hemispheric shifts in total EEG power during hypnotic analgesia that were interpreted as greater overall right-hemisphere involvement at the bipolar parieto-occipital region. Also using cold pressor pain, Crawford (1990b) found only highly hypnotizable individuals exhibited hemispheric asymmetries of high theta when attending (left > right) and ignoring pain (right > left) in the anterior temporal region whereas low hypnotizable participants showed no hemispheric asymmetries and no shifts between conditions (Crawford, 1990b, 1994). Hemispheric shifts were previously interpreted as specific hemispheric dominance for hypnotizability (e.g., Gur & Gur, 1974) and more recently as task specific (Crawford & Gruzelier, 1992; Crawford et al., 1996; Jasiukaitis, Nouriani, Hugdahl, & Spiegel, 1997; MacLeod-Morgan, & Lack, 1982). Crawford et al. (1996) proposed that the hemispheric shifts of higher theta power possibly reflects underlying hippocampal-cortical shifts of activity mediating neurophysiological influences of hypnotizability. Such hemispheric differences in EEG activity suggests there may be underlying morphological hemispheric differences between low and highly responsive individuals in those structures (e.g., corpus callosum, anterior cingulate, and other anterior frontal regions) associated with attentional and inhibitory processes.

### Hypnosis Studies of Attention

Various behavioral and physiological hypnosis studies have focused on attentional differences between low and highly hypnotizable individuals. As discussed in the prior section, hemispheric lateralization and specialization differences may be observed between the groups. At the behavioral level, attentional performance differences are noted in waking (Atkinson & Crawford, 1992; Crawford, 1981; Crawford, Brown & Moon, 1993; Priebe & Wallace, 1986; Wallace, 1986, 1988; Wallace, Allen, & Weber, 1994) or hypnotic (e.g. Crawford, 1996; Crawford & Allen, 1983; Crawford, Nomura, & Slater, 1983, Dywan & Bowers, 1983; Walker, Garrett, & Wallace, 1976; Wallace, 1978) conditions.

Crawford (1996) suggests that it may be the involvement of a more effective anterior

frontolimbic system in highly hypnotizable individuals that underlies their enhanced attentional and imaging ability differences. She suggested that shifts of attention and disattention, as well as sustained attentional or disattentional processing, influence the imaging abilities and may be due to efficiency differences in the anterior frontolimbic system. She further proposed that a more effective frontolimbic attention-disattention system in highly hypnotizable individuals contribute to their abilities to produce hypnotic analgesia. Crawford (1996) proposed that hypnotic analgesia involved the anterior frontal cortex in an “inhibitory feedback circuit that cooperates in the regulation of thalamocortical activities” (pp. 269).

Prior research identified differences in neurophysiological activity during hypnotic analgesia. During hypnotic analgesia, highly hypnotizable individuals demonstrated increased rCBF in the anterior frontal (orbitofrontal) and somatosensory regions of the brain (Crawford, Gur, et al., 1993). Decreased anterior cingulate activation with continuing, although somewhat different, activation of the anterior frontal regions was observed in our fMRI research (Crawford, Horton, Harrington, et al., 1998; Downs et al., 1998). Rainville and his associates obtained somewhat differing results. During hypnotic analgesia highly hypnotizable participants demonstrated decreased regional cerebral blood flow (rCBF) in the anterior cingulate (Rainville et al., 1997, 1999) and anterior frontal regions (Rainville et al., 1999).

During hypnotic analgesia, studies of somatosensory ERPs have shown only highly hypnotizable participants exhibited early time-locked effects in the anterior frontal region that suggests early re-allocation of attention whereas later time-locked effects were observed more posteriorly, reflecting their self-reported lack of involvement in the assessment of stimulus intensity and body part location (e.g., Crawford, Knebel, Kaplan, et al., 1998; Crawford, Knebel, Vendemia, & Horton, in press). In a study involving intracerebral recordings (Kropotov et al., 1997), decreased positive ERP activity was recorded in the anterior cingulate and enhanced negative ERP activity in the anterior temporal region during hypnotic analgesia.

Electrophysiological recordings of highly hypnotizable individuals also indicate shifts in hemispheric dominance of neurophysiological activity during hypnotic analgesia. There is a shift in hemispheric dominance of theta EEG power in the temporal region (Crawford, 1990b). Highly hypnotizable individuals also demonstrate greater negativity, reduced

positivity and increased neural processing speed, during attend conditions, in electrophysiological studies with some hemispheric differences (Crawford, Horton & Lamas, 1998; Horton et al, 1998).

The more effective use of attentional resources and processing of information by highly hypnotizable individuals, as observed behaviorally and electrophysiologically, suggest underlying neurophysiological or neuroanatomical differences between individuals who are and are low hypnotizable. These differences are particularly suggested in the anterior frontal region and associated brain structures implicated in attentional and inhibitory processing. This study measured the CC, the anterior cingulate, and the forebrain to determine if there are differences in the volume of brain structures between highly hypnotizable individuals and low hypnotizable individuals.

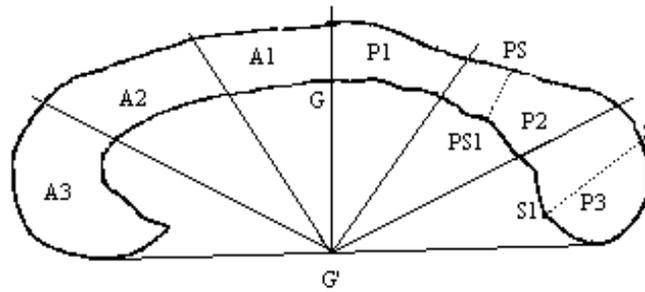
#### Summary of Research

There is empirical evidence for a relationship between hypnotic level and attentional processing. Furthermore, increased lateralization in individuals who are highly hypnotizable has been reported in various studies. Another research line indicates that lateralization of morphological differences in the anterior cingulate may be related to attention performance. Research also indicates a relationship between CC functioning and behavioral and attentional processes as well as neurophysiological differences in fiber diameters, location and density in the CC and related differences in IHTT. Morphological differences in CC volume has also been positively correlated with forebrain volume. The combinations of relationships with hypnotizability, attention, lateralization, neuroanatomical and neurophysiological differences of the CC, as well as differences in IHTT, suggest that individuals who differ in hypnotizability abilities also differ in IHTT latency measures that are possibly correlated with neuroanatomical differences of the CC. These differences may also be correlated with the neurophysiological functioning of the CC.

Table 2.1  
Corpus Callosum Regions of Division

<u>Region of Division</u>	<u>Area Designation</u>	<u>Proposed Cortical projection</u>
Rostrum	1	Caudal, Orbital prefrontal, Inferior premotor
Genu	2	Dorsolateral Prefrontal
Rostral body	3	Premotor, Supplementary motor
Anterior mid-body	4	Motor
Posterior mid-body	5	Somesthetic, Posterior parietal
Isthmus	6	Superior temporal, Posterior parietal
Splenium	7	Occipital, Inferior temporal

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Schematic of CC division adapted from Clarke et al. (1989)

- G Designates the “center of gravity” as mathematically calculated  
(See Clarke et al., 1989 for a review)
- G’ Designates the projection of the “center of gravity” onto an anterior-posterior baseline joining the most inferior points of the CC. The CC is divided into six regions by 30-degree intervals from this point.
- A1 Anterior mid-body – defined as the anterior half minus the anterior third of the CC.  
(Approximately analogous to the straight-line division comprising the anterior mid-body)
- A2 Anterior body – defined as the anterior third minus the anterior fifth of the CC.  
(Approximately analogous to the straight-line division comprising the rostral body and a portion of the genu)
- A3 Genu and rostrum – defined as the anterior fifth of the CC.  
(Approximately analogous to the straight-line division comprising most of the genu and the rostrum)
- P1 Posterior mid-body – defined as the posterior half minus the posterior third of the CC.  
(Approximately analogous to the straight-line division comprising the posterior mid-body)
- P2 Posterior isthmus – defined as the posterior third minus the posterior fifth of the CC.  
(Approximately analogous to the straight-line division comprising the Isthmus and a portion of the anterior area of the splenium)
- P3 Splenium – defined as the posterior fifth of the CC.  
(Approximately analogous to the straight-line division comprising the majority of the splenium)
- PS-PS<sub>1</sub> (superior presplenial – inferior presplenial at the area of least thickness) Used as T<sub>min</sub>
- S-S<sub>1</sub> (superior splenium – inferior splenium: at the largest dimension)

The bulbosity of the CC is defined as the dimension across the widest portion of the splenium of the CC.

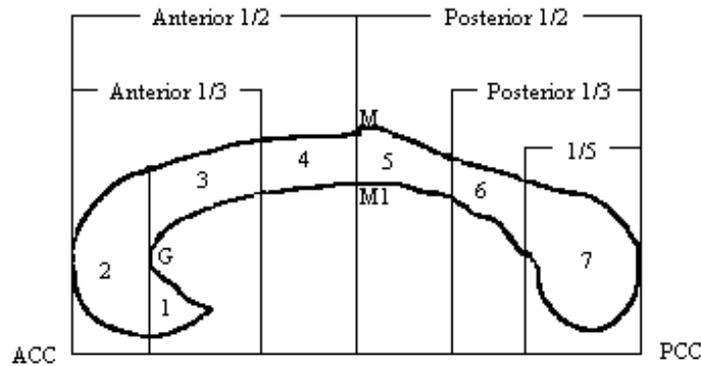
Bulbosity index – A calculation of the bulbosity of the splenium using Clarke et al.’s (1989) formula

$$\frac{T_{\max} - T_{\min}}{T_{\min}}$$

where T<sub>max</sub> is the maximum thickness of the splenium and T<sub>min</sub> is the minimum thickness of the presplenial region.

**Figure 2.1**

**Radial Method of Corpus Callosum Division.**



Schematic of CC division based on Witelson (1989)

ACC-PCC (anterior corpus callosum – posterior corpus callosum)

The length of the CC is defined as the dimension from the most anterior portion of the CC to the most posterior portion of the CC.

G The most anterior division of the CC at the posterior bend of the genu

M-M<sub>1</sub> (superior mid-body – inferior mid-body)

The thickness of the mid-body is defined as the dimension from the most superior part of the mid-body of the CC to the most inferior part of the mid-body of the CC.

1. The genu is defined as the most anterior portion of the CC beginning with the interior convexity and extending anteriorly. The genu contains callosal fibers related to the anterior frontal cortex.
2. The rostrum is located ventral to the body of the CC and is the posterior extension of the genu. The rostrum contains callosal fibers related to the caudal/orbital, anterior frontal, and inferior premotor cortex.
3. The rostral body is defined and the anterior third of the CC less the genu and contains fibers related to premotor and supplementary motor cortex.
4. The anterior mid-body is defined as the anterior half less the anterior third of the CC and contains fibers related to the motor cortex.
5. The posterior mid-body is defined as the posterior half less the posterior third of the CC and contains fibers related to the somatosensory and posterior parietal cortex.
6. The isthmus is defined as the posterior third less the posterior fifth of the CC and contains fibers related to the superior temporal and posterior parietal cortex.

The splenium is defined as the posterior fifth of the CC and contains fibers related to the occipital and inferior temporal cortex.

Figure 2.2

Straight-Line Method of Corpus Callosum Division.

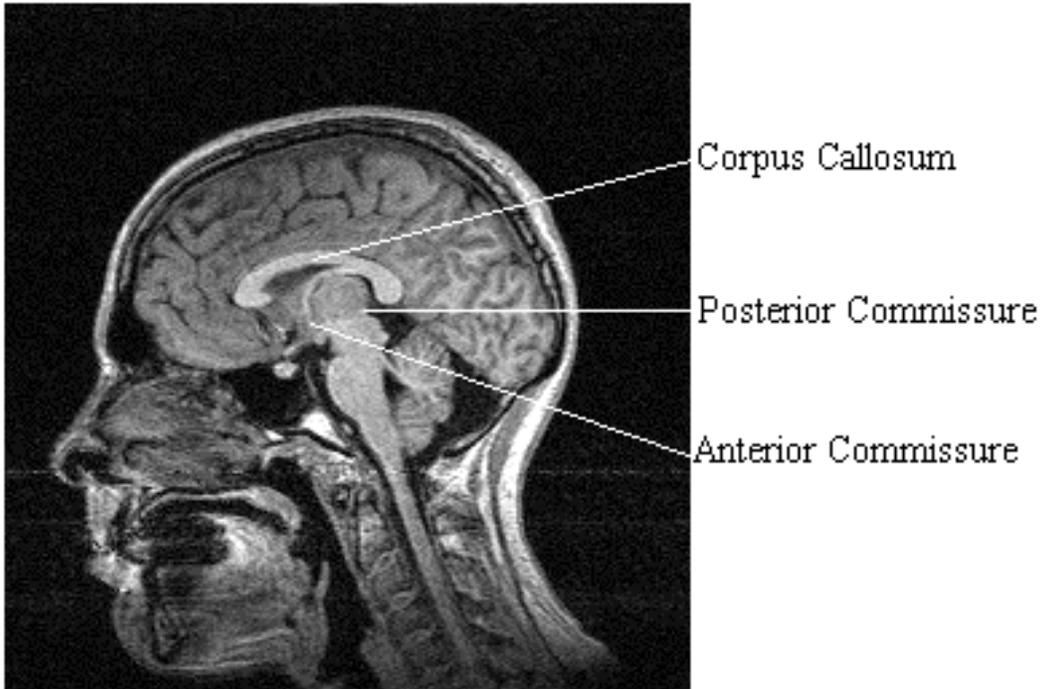


Figure 2.3  
Midsagittal Image Illustrating the Anatomical Location of the Anterior  
Commissure, Posterior Commissure, and Corpus Callosum.

## CHAPTER 3

### PURPOSE AND RATIONALE OF CURRENT STUDY

This study extends the ongoing fMRI research by using the anatomical MRIs of low and highly hypnotizable individuals to investigate hypothesized morphological differences of the CC and anterior cingulate. The morphological differences may be correlated with neurophysiological activity associated with the more effective allocation of resources (for reviews, see Crawford, 1994a, 1994b; Crawford & Gruzelier, 1992) and the faster neural processing speed (Crawford, Horton, & Lamas, 1998; Horton et al, 1998) observed in highly hypnotizable individuals. It is unclear whether the more effective neural processing exhibited by highly hypnotizable individuals is due to a neurophysiological influence, strategies, or an interaction with neurophysiological influences and strategies used by those individuals.

This study tested the hypothesis that the more effective inhibitory processing of pain is correlated with a neurophysiological influence. The increased size of the CC has been hypothesized to be a neuroanatomical indicator of more effective interhemispheric transfer of information (e.g., de Lacoste-Utamsing & Holloway, 1982; Witelson, 1985). This study analyzed CC size to investigate the existence of neurophysiological differences in low vs. high hypnotizables. Some studies showed sex differences in CC size (e.g., Davatzikos & Resnick, 1998; de Lacoste-Utamsing & Holloway, 1982; Going & Dixson, 1990; Holloway & de Lacoste, 1986; Witelson, 1989) while other studies did not (e.g., Byne et al., 1988). Therefore, this study also analyzed CC size as a possible neurophysiological difference between men and women.

#### Hypnotizability and Anterior Regions of the Corpus Callosum

Increased volume of a particular region of the CC is an indirect indicator of increased diameter or myelination of the neurons in that particular region of the CC, and increased diameter or myelination of neurons correlate with increased (faster) neural processing (e.g., de Lacoste-Utamsing & Holloway, 1982; Witelson, 1985). Faster neural processing should result in faster activation of inhibitory circuits and more effective behavioral inhibition that is

reported in highly hypnotizable individuals.

Therefore, the first purpose of this study was to evaluate the size of anterior regions of the CC in low and highly hypnotizable individuals. It was anticipated that the greater efficiency in inhibiting pain among highly hypnotizable participants would correlate with increased CC volume in the anterior regions of the CC. The anterior frontal region of the brain (BA 9 & 10) is involved in inhibitory processing in highly hypnotizable individuals (Crawford, Horton, Harrington, et al., 1998; Downs et al., 1998). The topographic projections of the CC for the anterior frontal region of the brain are proposed to be in the rostrum and genu of the CC. Therefore, it was anticipated that the anterior regions of the CC would be larger in highly hypnotizable individuals as compared with low hypnotizable individuals.

#### Hypnotizability and the Mid-body of the Corpus Callosum

A consistent finding in the literature is that highly hypnotizable individuals exhibit faster response times in identifying visual field stimuli (Crawford et al., 1995) and during simple and complex decision making tasks (e.g., Acosta & Crawford, 1984; Saccuzzo, Safran, Anderson, & McNeill, 1982). Furthermore, as reviewed earlier, highly hypnotizable individuals have faster auditory and somatosensory ERP components suggestive of faster information processing than low hypnotizables. Decreased diameter or myelination of neurons correlates with decreased (slower) neural processing that delays activation of inhibitory circuits and results in less effective behavioral inhibition (de Lacoste-Utamsing & Holloway, 1982; Witelson, 1985). The less effective behavioral inhibition could result in faster reaction times to stimuli received in the somatosensory cortex.

Therefore, the second purpose of this study was to evaluate the mid-body of the CC for volume differences between low and highly hypnotizable individuals. It was anticipated that faster response of highly hypnotizable individuals may be due to less effective inhibition caused by a slower IHTT and consequently would be correlated with a smaller CC size in the posterior mid-body. An alternative hypothesis would be that increased reaction times by either left or right hands to lateralized visual field presentation (Crawford et al., 1995) would be reflected in a larger CC size in the posterior mid-body.

## Relationships of Corpus Callosum Size to Other Brain Structures

Research investigating the relationship of CC size to other brain structures has been of interest to a few researchers. Ringo et al. (1994) reported a negative relationship between CC size and total brain volume with individuals with a larger CC having a smaller total brain size. However, Jäncke et al. (1997) reported a positive relationship between CC size and forebrain volume with individuals with larger CCs also having larger forebrain size.

The third purpose of this study was to evaluate the relationship of CC size to other selected brain structures (e.g., frontal brain area) and the size of the medial cortex. The frontal area of the cortex is associated with inhibitory functioning via the limbic lobe, and the CC is associated with inhibitory activity involving interhemispheric integration of information. A larger CC size is associated with more effective interhemispheric communication that would result in the facilitation of frontal lobe activity by inhibition of inhibitory neurons in the frontolimbic system. Therefore, it was anticipated that highly effective inhibition, such as exhibited by highly hypnotizable participants in this study, would be reflected in both larger anterior CC size and a larger frontal cortical area.

Since Ringo et al. (1994) reported that individuals with larger CC have smaller total brain volumes, it was anticipated there would be a positive correlation between larger anterior CC size and larger forebrain volume but not with overall medial cortex volume. The present study limited its analyses of cortical areas to three images, one midsagittal image and one adjoining image from each hemisphere of each participant. Therefore, references to the medial volume of the overall cortex, the forebrain area and the anterior cingulate is a product of the area of each of three images in square pixels by the thickness of each image in millimeters. References to cortical size or volume by studies using MRI technology (e.g. Byne et al., 1988; Clarke & Zaidel, 1994; Jäncke et al., 1997) and postmortem or other studies (e.g. Going & Dixon, 1990; Ringo et al., 1994; Witelson, 1985, 1989; Witelson & Goldsmith, 1991) must be qualified with limited similarity for comparison.

## Hypnotizability and the Anterior Cingulate

There are reported relationships of the anterior cingulate to attention (Casey et al., 1997; Kolb & Whishaw, 1996; Posner, 1995; Vogt et al., 1992), and there is an extensive literature identifying more effective attentional processes in highly hypnotizable individuals (for a review, see Crawford, 1994a, 1994b). Therefore, the fourth purpose of this study was to evaluate differences in anterior cingulate size between low and highly hypnotizable individuals. This study also evaluated the relationship of the anterior cingulate area to total cortex area at the midsagittal region of the brain.

## Sexual Dimorphism and the Corpus Callosum

Quite inconsistently across studies, there is a suggestion of sex differences in the size of the CC. Research investigating sexual dimorphism are mixed and include findings by de Lacoste-Utmasing & Holloway (1982) and Holloway & de Lacoste (1986) of a larger splenium in women which was attributed to the difference in visuospatial skills of men and women. In contrast, other research (Byne et al., 1988; Clarke & Zaidel, 1994) failed to replicate the finding of a larger splenium in women. Larger CC regions are associated with more effective inhibition and increased hemispheric specialization while smaller CC regions are associated with less effective inhibition that results in increased interhemispheric activity and less hemispheric specialization.

Therefore, the fifth purpose of this study was exploratory. It evaluated the posterior regions of the CC between men and women and between low and highly hypnotizable individuals to determine if there were any consistent differences that may be explained by a theoretical approach to neural functioning.

## Hypotheses

### Hypothesis One

Due to more effective inhibitory processing in highly hypnotizable individuals that is associated with the anterior frontal region of the brain and anterior third of the CC, it was hypothesized that the anterior regions of the CC would be larger in highly hypnotizable individuals than in low hypnotizables. Specifically, it was hypothesized that regions of the anterior third of the CC that project topographically to areas of the anterior frontal region of the brain (e.g., BA 8, 9 & 10), and include the rostrum, genu, and anterior portion of the rostral body, would be larger in highly hypnotizable participants than in low hypnotizable participants.

### Hypothesis Two

Highly hypnotizable individuals have faster reaction times (e.g., Acosta & Crawford, 1985; Crawford, Kapelis, & Harrison, 1995; Saccuzzo et al., 1982) and faster latencies of somatosensory and auditory ERP components (Crawford, Horton, & Lamas, 1998; Crawford et al., under review; Lamas & Crawford, 1998; Lamas et al., under review; Horton et al., 1998; McClain-Furmanski, et al., 1999). Less effective inhibitory processing could result in increased behavioral response such as reaction time. Smaller volume in the CC would indicate less effective IHTT and subsequently less effective inhibitory processing. Therefore, it was hypothesized that the mid-body regions of the CC involved in somatosensory processing and motor processing would be smaller in highly hypnotizable individuals. Specifically, it was anticipated that the posterior mid-body of the CC would be smaller in highly hypnotizable participants than in low hypnotizable participants. Yet, an alternative hypothesis would be that increased reaction times by either left or right hands to lateralized visual field presentation (Crawford, Kapelis, & Harrison, 1995) found among highly hypnotizable individuals would be reflected in a larger CC size in the posterior mid-body.

### Hypothesis Three

A larger CC size is associated with more effective interhemispheric communication and facilitation of frontal lobe activity. Therefore, it was anticipated that effective inhibition associated with anterior frontal brain activity would be reflected in both larger anterior CC size and a larger frontal cortical area. Therefore, it was hypothesized that there would be a positive correlation between the anterior CC size and frontal brain size for both low and highly hypnotizable individuals with individuals who have a larger anterior region of the CC also exhibiting larger overall frontal brain volume.

### Hypothesis Four

A larger anterior cingulate size in the right hemisphere of the brain has been associated with better attentional performance (Casey et al., 1997). Highly hypnotizable individuals exhibit more effective attentional abilities (for a review, see Crawford, 1994a, 1994b) and recent research (Casey et al., 1997) has suggested a positive correlation between right anterior cingulate size and attentional abilities. Thus, it was hypothesized that highly hypnotizable individuals would have a significantly larger anterior cingulate (defined as BA 24 for this analysis) in the right than left hemisphere and that low hypnotizables would not show hemispheric differences.

## CHAPTER 4

### METHOD

#### Participants

The university student participants, aged 18 to 29, were eight highly hypnotizable individuals (four women and four men; SHSS:C  $M = 11.0$ ,  $SD = 1.07$ ), and 10 low hypnotizable individuals (five men and five women; SHSS:C  $M = 2.1$ ,  $SD = .88$ ). The participants reported being in excellent health and reported no history of concussion or other medical history that might interfere with neurophysiological processing. The participants were stringently selected on several criteria to be discussed below.

#### Preliminary Screening of Participants

##### Hypnotic Assessment

The participants were asked not to participate if they were presently in counseling, psychotherapy or psychotropic drug treatment. Approximately 300 participants participated in two separate sessions that screened for hypnotic susceptibility. The participants were administered two hypnotic susceptibility scales in small groups (10-40) in a university classroom by a trained graduate student (this researcher and others) or Dr. Helen Crawford from the Neurocognition Laboratory at Virginia Polytechnic Institute and State University.

Following a 10 minute discussion of hypnosis and its common uses, the participants were first administered the 12-item Harvard Group Scale of Hypnotic Susceptibility, Form A (Shor & Orne, 1962). Within the following two weeks the participants were administered the group version (Crawford & Allen, 1982) of the 12-item Stanford Hypnotic Susceptibility Scale, Form C (SHSS:C; Weitzenhoffer & E. R. Hilgard, 1962); the group version contains the same suggestions as the individual SHSS:C and is revised for group administration. In both scales, all mention of drowsiness and sleep were replaced with relaxation. For samples drawn from the same university population, typical correlations between the HGSHS and SHSS:C range

from mid to high .70s (Galper, 1999; Lyons & Crawford, 1997). The participants considered to be highly hypnotizable individuals consisted of those who scored high (9-12) on the two hypnotic susceptibility scales, while the individuals selected as not being hypnotizable consisted of those who scored low (0-4) on the two hypnotic susceptibility scales. The participants were invited to return for training in pain control if they met further criteria.

### Cold Pressor Training

The participants were further screened for participation in cold pressor pain control training. The participants were administered the Beck Depression Inventory (BDI) and were selected to participate in the study only if they scored low (less than 10) on the BDI. The participants were also strongly right-handed, as assessed by the Annett (1967) Handedness Scale, with no left-handed or ambidextrous close relatives. They reported no use of tobacco, no known medical or psychiatric problems, cardiac problems, chronic obstructive pulmonary disease, arthritis or joint disorders, labile hypertension, Raynaud's disease, peripheral circulatory problems or major skin disorders other than acne. They also reported no past chronic pain episodes. They were not taking any medications (except birth control pills for some of the women).

The participants were trained to reduce or eliminate the perception of pain and distress as is typically done in the literature (E. R. Hilgard & J. R. Hilgard, 1994) with the cold pressor test. The cold-pressor pain apparatus consisted of a large insulated cooler filled with water and enough crushed ice to maintain a recorded temperature of 0 – 1° C. Each participant had the procedure explained, was again evaluated for past medical history, and was asked to sign a consent form. The participant was then asked to place their left hand into the container of crushed ice and water for 60-second periods in each of the following conditions: waking attend, hypnosis attend, and hypnosis with suggested analgesia (three times). Prior to each dip, the experimenter stirred the crushed ice.

The participants were asked to rate their sensory pain and their emotional distress on scales ranging from 0 for no pain (distress) to 5 for moderate pain (distress) and 10 for unbearable pain (distress). The participants were allowed to rate their pain (distress) higher

than 10 on an open-ended scale to represent greater pain (distress) (E. R. Hilgard & J. R. Hilgard, 1994). The participants were given permission to remove their hand from the water and ice at any time if the pain became too intense.

Each participant was asked to place their hand into the water for an initial time of 30 seconds to teach them how to rate pain and distress and to acclimate them to the procedure. Prior to the hypnosis induction each participant was asked to attend to their left hand as it was placed into the water and ice for 60 seconds; they rated their pain and distress every 10 seconds. Each participant was then hypnotized and during hypnosis, they were asked to attend to their hand and rate their pain and distress every 10 seconds during one 60-second dip. Each participant was then taught hypnotic analgesia techniques, including suggestions of the hand and arm being numb and insensitive, and imagining a place such as the mountains or beach at which they would like to be. Three 60-second training dips occurred with participants reporting any pain or distress every 10 seconds. After the first two training dips, participants who reported successful strategies were asked to incorporate these strategies into the next training dip.

Only these highly hypnotizable participants who were able to eliminate all perception of pain and distress during cold pressor training were selected to participate in subsequent studies, assessing the neurophysiology of pain and hypnotic analgesia. Low hypnotizable individuals who could or could not reduce pain or distress perception were invited to participate; no low hypnotizable individuals were able to eliminate the perception of pain.

### Additional Screening of Participants

#### Criteria for Participation in the Neuroimaging Study

Prior to participation in MRI acquisition, the participants were required to meet further screening criteria. The highly hypnotizable participants must have been able to completely reduce pain and distress during cold pressor training. They reported 0 (for no pain and no distress) after a 60-second immersion of their hand and forearm in 0 – 1° C water and crushed ice during hypnotic analgesia. The participants were questioned further and all reported no

evidence of claustrophobia for small spaces, and no learning disabilities or attention deficit disorder. They were also questioned regarding any metallic content in their bodies and reported no metallic content. They were instructed to refrain from alcohol use, illegal drugs (e.g., marijuana), and over-the-counter or prescribed drugs for 24 hours prior to the fMRI study. It was verified that none smoked or chewed tobacco.

The participants involved in the fMRI study traveled to the Neurovisualization Laboratory at the University of Virginia Medical School to participate in the study. The participants received lunch prior to the experiment and \$100.00 for participating in the experiment. Upon arrival, the participants were further introduced to the study and signed consent forms. The participants were fitted with a molded plastic mask that encompassed their face and allowed their head to be securely affixed in a shielded, elliptical, radio frequency (RF) coil designed for high-sensitivity brain imaging. The molded plastic mask was necessary for reducing head movement.

The participants then were transported to the nearby MRI facilities at the University of Virginia Medical School. They were briefed on the procedures of the experiment. They were placed on the moveable bed of the scanner in a supine position and had the molded plastic mask placed over their head. After the participants were comfortable and relaxed, they were moved into the scanner.

The anatomical MRI was procured for the purpose of registry of the succeeding fMRI scans. The anatomical MRI for each participant included a sequence of 128 sagittal images taken perpendicular to the anterior commissure-posterior commissure (AC-PC) line. The anatomical MRI was acquired using a 1.5 Tesla Siemens Vision scanner with the magnetization prepared rapid acquisition gradient echo (MPRAGE) protocol to acquire three dimensional T1 weighted images with a field of view (FOV) of 256 mm. The image slices were 1.8 mm thick with an in-plane resolution of 1.1 mm by 1.1 mm that extended from the most superior aspect of the brain through the most inferior aspect of the brain.

### Image Selection and Preparation

The anatomical MR images from the Siemens Vision Scanner were used for the

measurement and analyses of brain structures of the participants. The midsagittal image of each participant was chosen based on the appearance of the medial gyri and sulci and the location of the septal pellucidum. To accommodate for any variation in the selection of the midsagittal slice, the adjoining slices from the left and right hemispheres were also selected and all three slices were measured and the area recorded in square pixels. The midsagittal slices were selected independently by another trained researcher to establish interrater reliability for image selection.

Each image selected for analysis was realigned to the XY coordinates of the Scion Image (Scion Corporation) program, thus allowing the anterior and posterior commissures to align on the same horizontal plane as indicated by the Y coordinates of the Scion Image (Scion Corporation) program. The primary investigator recorded the XY coordinates of the anterior and posterior commissures prior to realignment and after realignment. The original image was rotated only once for realignment. If additional or less degrees of rotation were required for alignment, the original image was used for a new rotation to minimize the image distortion due to rotation.

The total area of the three selected contiguous image slices from each participant was summed and multiplied by the slice thickness of 1.8 mm to generate a product used in analysis of medial volume of several brain structures. The structures analyzed for medial volume included the forebrain, anterior cingulate, overall cortex, total CC, and regions of the CC including the rostrum, genu, rostral body, anterior mid-body, posterior mid-body, isthmus and splenium.

The total area of the CC was measured in the original image and the rotated image using the magic wand feature of the Scion Image (Scion Corporation) program with the threshold level set by default (threshold = 109 from the intensity range of 0 – 255 grayscale values). The required rotation ranged from –8.00 degrees to +16.00 degrees and the distortion of the CC resulted in an average reduction of .045 in the area of the CC after rotation. The total area of the CC was also measured in the original and rotated images by manually outlining the CC with an Ipen Pro (Cross Pen Computing Group) digital pen and measuring the outlined area. The distortion due to rotation was not as evident with the subjective determination of CC boundaries used with manual outlining and resulted in an average reduction of .014 in the area

of the CC. The default threshold and magic wand measurement rely on the Scion Image (Scion Corporation) program determining boundaries and outlining the structure. The resulting area is determined by measuring the pixels inside the identified boundaries. The manual outlining protocol also included the outer pixels of the boundary of the CC and resulted in a larger area that was more comparable with other brain structures such as the forebrain, anterior cingulate and total cortex that required manual outlining. All other brain structures of interest were outlined using the manual outlining method.

### Corpus Callosum Divisions

Several approaches to CC division (discussed earlier) have been used to investigate relationships of CC size. This study used the realigned images and divided the CC based on the radial method of division used by Clarke et al. (1989). An additional division of the rostrum was based on the straight-line method of division used by Witelson (1989).

The primary investigator magnified each image to eight times its original size prior to dividing the CC into regions. To accomplish the radial division, the primary investigator determined the center point of the CC by identifying the X coordinate of the XY location at the most anterior point of the genu and the X coordinate of the XY location at the most posterior point of the splenium. The anterior X coordinate of the XY location was subtracted from the posterior X coordinate of the XY location; this yielded a product that indicated the length of the CC in pixels. The center point of the CC was determined by dividing the length of the CC in half and adding the result to the X coordinate at the most anterior point of the genu. The resulting X coordinate of the center of the CC was transferred to a baseline XY location on a line drawn across the most inferior points of the anterior and posterior portions of the CC.

Radial lines at 90 degrees, 30 degrees and 60 degree intervals were drawn from the relocated center point on the baseline to intersect the CC and divide it into six sections as detailed in Figure 2. The rostrum was then separated by a perpendicular line located at the most posterior point of the curve of the genu just inferior to the rostral body and extending from the curve of the genu inferior through the rostrum. After the division of the CC for all

images, the investigator again measured the angle of intersections for the lines at 90 degrees, 30 degrees, and 60 degrees and recorded the measured angles. The difference of the measured angles as compared to the ideal angles of 90 degrees, 30 degrees, and 60 degrees was calculated as a difference score for each angle of each image and averaged for a primary rater consistency measure.

### Measurements of Brain Structures and Areas

The primary investigator was blind to all conditions and participants. All participants were coded and all measurements of images were done by the primary investigator without knowledge of the identity of the participants or their hypnotic susceptibility level.

The measurements of brain structures were made using the Scion Image (Scion Corporation) program that was developed by the National Institutes of Health and is made available to researchers in the field. The area of interest was outlined manually and measured by the Scion Image (Scion Corporation) program using pixel summing.

Each region of the CC was measured and the pixels of the division line added to the product for a total area of each region. Each image was magnified to eight times its original size prior to measuring the regions and the total CC. The thickness of the CC was measured at the center point of the CC, and the splenial width was measured at the widest point of the splenium. The minimum thickness in the posterior half of the CC that was presplenial was measured and used along with the splenial width to calculate a bulbosity index using the formula of Clark et al. (1989). For all measurements, a minimum of three measurements and a maximum of five measurements were recorded. The average of the measurements was used as the area of the region of interest. The difference was calculated between the least measurement and the largest measurement and converted to a percentage of difference of measurement. This percentage of difference was recorded for each region of interest and used as the primary rater consistency check.

The total area of the CC was manually outlined and the Scion Image (Scion Corporation) program was used to measure the outlined area. The measured area of the total CC was recorded and compared to the summation of the measured regions of the CC. The difference

between the summation of the measured regions and the measured area of the total CC was compared and a difference score calculated as a primary rater consistency check. The summation of measured regions was used as the total CC area for statistical analyses of the data.

### Forebrain

The forebrain was measured for each image by manually outlining the cortex from a point perpendicular from the precentral sulcus (as the posterior limit of the forebrain) to the callosal sulcus of the CC. This included all cortical area anterior of this posterior limit and superior to the callosal sulcus. The total cortex was measured for each image by manually outlining all of the cortical area visible in the sagittal image superior to the callosal sulcus of the CC and cerebellum. The perimeter of the forebrain area and cortex measured included the visible meninges.

Originally it had been planned that the anterior cingulate would include BA 24 and 32, but this was not possible. The resolution of the anterior cingulate at the selected medial images was not consistent enough to consistently identify BA 32 reliably. Thus, the anterior cingulate was measured for each image by manually outlining only BA 24. The primary investigator used the same procedure of a minimum of three measurements and a maximum of five measurements that were recorded and rater consistency calculated for all areas of interest.

### Interrater Reliability

The primary investigator and an independent rater, a trained graduate student at Virginia Polytechnic Institute and State University, were blind to the participants' hypnotizability and sex. To determine interrater reliability of image selection, the primary investigator and independent rater each independently identified the midsagittal image and one adjoining image from either hemisphere for each participant. Interrater reliability for measurement was assessed on one third of the total images consisting of one image from each participant. The

images used for measurement reliability were randomly selected from the left hemisphere, the midsagittal slice or the right hemisphere of each participant. Separately from the primary investigator, the independent rater used the Scion Image (Scion Corporation) program and measured the area of the forebrain area, overall cortex area, anterior cingulate, total CC area, maximum splenium width, and minimum presplenial thickness. The total CC area was used as a reliability measure in place of each section of the CC since the independent rater compared one measure of the total CC to the summation of sections of the CC measured by the primary investigator.

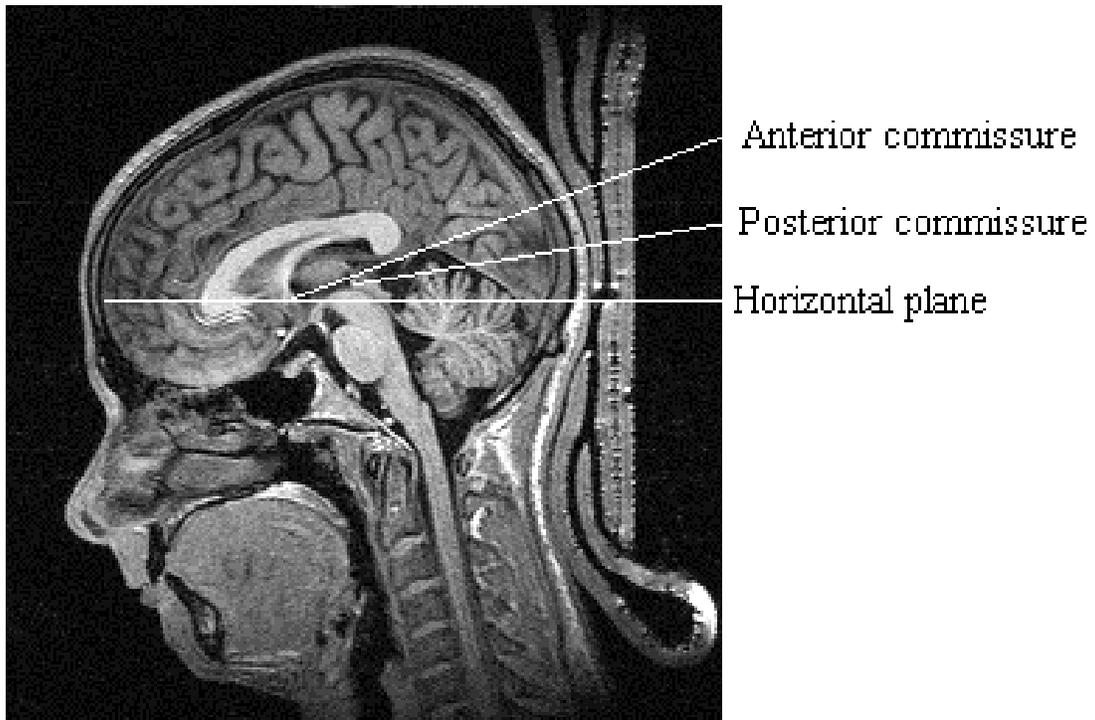


Figure 4.1

MRI Midsagittal Image:

Before Realignment to a Horizontal Plane by the Anterior and Posterior Commissures.

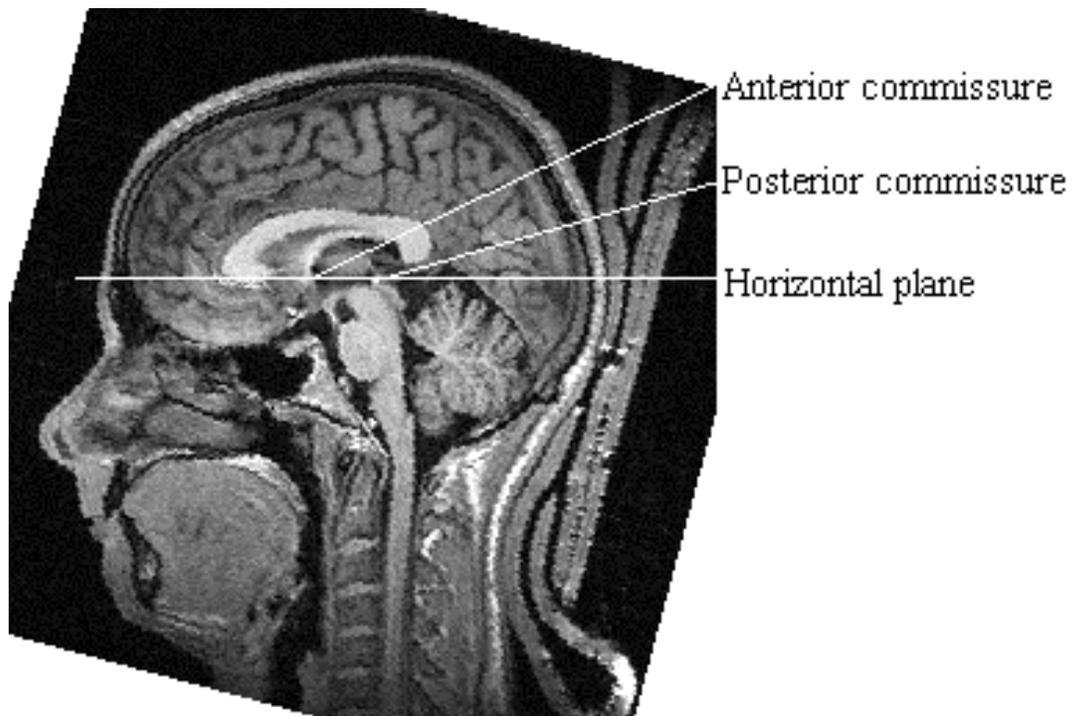


Figure 4.2

MRI Midsagittal Image:

After Realignment to a Horizontal Plane by the Anterior and Posterior Commissures.

## CHAPTER 5

### RESULTS

#### Primary Investigator Consistency

The primary rater and independent rater recorded a minimum of three measurements and a maximum of five measurements for each region of interest. The measurements were averaged and used for comparison of interrater reliability and for statistical analyses. The primary rater's consistency was determined by calculating a difference score between the smallest and largest measurements and dividing the difference score by the largest measurement yielding a percentage of consistency for measurements.

The primary investigator had a measurement consistency of .992 for the forebrain area, .994 for the overall cortex, and .976 for the anterior cingulate. This yielded an overall 98.7 percent consistency for the cortical areas of interest.

The consistency of angle division of the CC was 1.00. The measurement consistency for the regions of the CC were .999 for the rostrum, .989 for the genu, .988 for the rostral body, .990 for the anterior mid-body, .987 for the posterior mid-body, .987 for the isthmus, .992 for the splenium, and .987 for the total CC. The consistency of agreement between the total CC measurement and the summation of CC regions was .999. The measurement consistency was 1.00 for the mid-body thickness, .998 for the splenium width, and 1.00 for the presplenial thickness. The average consistency for CC measurement was 99.3 percent. The overall average consistency of measurement for all regions of interest by the primary investigator was 99.3 percent.

#### Interrater Reliability

Interrater reliability was checked by two methods: (1) Pearson rs were calculated between the measurements of the primary investigator and the independent rater, and (2) difference scores were calculated between their measurements. The difference scores were transformed into absolute difference scores and divided by the primary investigator's original

measurement to yield a percentage of difference for each image. The average of all images yielded an overall difference percentage of measurement for each cortical region measured. The percent of agreement between the primary investigator and the independent rater is reported for each cortical region measured.

Independently, the primary investigator and the independent rater each selected the midsagittal image and adjacent images from the left and right hemispheres of each participant. The primary investigator and independent rater only disagreed on image selection by one adjacent image of the set of three images for three participants (e.g., primary investigator selected images 67, 68, and 69, while the independent rater selected images 68, 69, and 70). The interrater reliability for image selection was 94%.

The interrater reliability for measurements of overall cortex area was  $r = .97$ ,  $p < .0001$ , with the absolute difference score showing 98% agreement. The interrater reliability for measurements of the forebrain area was  $r = .92$ ,  $p < .0001$ , with the absolute difference score showing 97% agreement. The interrater reliability for measurements of the anterior cingulate was  $r = .995$ ,  $p < .0001$ , with the absolute difference score showing 97% agreement. The interrater reliability for measurements of the CC was  $r = .95$ ,  $p < .0001$ , with the absolute difference score showing 96% agreement. The interrater reliability rating for measurements of the maximum splenium width was  $r = .75$ ,  $p < .001$ , with the absolute difference score showing 94% agreement. The interrater reliability for measurements of the minimum presplenial thickness was  $r = .79$ ,  $p < .001$ , with the absolute difference score showing 89% agreement. The overall interrater reliability was  $r = .999$ ,  $p < .0001$ , with the absolute difference scores showing 95% agreement between measurements of the primary investigator and the independent rater.

## Morphological Differences in the Corpus Callosum

### Total Medial Corpus Callosum

A mixed factorial ANOVA for a nested design [2 (hypnotic level) X 2 (sex) X 2 (images: left hemisphere, right hemisphere)] was conducted. There were no significant differences in

the total medial volume of the CC between low and highly hypnotizable participants. There were no significant differences in sex, hemisphere or interaction between variables for the total medial volume of the CC.

### Corpus Callosum Regions

For each CC area, a mixed factorial ANOVA for a nested design [2 (hypnotic level) X 2 (sex) X 2 (images: left hemisphere, right hemisphere)] was conducted. As predicted, there were significant volume differences between low and highly hypnotizable participants in some regions of the CC. Furthermore, there were some hemispheric differences. Consistently, no significant sex differences in CC volume were observed. The following subsections provide analyses for each CC section.

#### Anterior Third of Corpus Callosum

It was hypothesized that there would be significant differences between low and highly hypnotizable participants CC regions in the anterior third of the CC: rostrum, genu, and rostral body. As presented below, the hypothesis was partially supported. There was a significant difference in rostrum volume between low and highly hypnotizable participants, but no significant differences were observed in the genu and rostral body CC regions.

Rostrum corpus callosum region. As predicted, there was a highly significant main effect for hypnotizability. As shown in Figure 5.1, highly hypnotizable participants had a significantly larger rostrum volume than did low hypnotizable participants, [Highs:  $M = 550.7$ ,  $SD = 82.2$ ; Lows:  $M = 502.6$ ,  $SD = 81.9$ ;  $F(1,7) = 12.90$ ,  $p < .009$ ]. Within groups, there was no significant main effect for sex in the rostrum volume. Also, the interaction between hypnotic susceptibility and hemisphere was not significant. However, there was a significant hemisphere difference [ $F(1,7) = 5.575$ ,  $p < .050$ ] with the mean rostrum volume in the right hemisphere ( $M = 43.7$ ,  $SD = 20.9$ ) larger than the left hemisphere ( $M = 54.5$ ,  $SD = 29.0$ ). The hemispheric differences are analyzed further and reported in more detail in a later

section of post hoc exploratory analyses. The significant differences for the rostrum are summarized in the ANOVA source table for the rostrum in Table 5.1.

Genu corpus callosum region. Contrary to the hypothesis that there would be differences in the anterior third of the CC, there was no significant difference in the volume of the genu between low and highly hypnotizable participants. Also, within groups, there were no significant main effects for sex or hemisphere. Finally, there was no significant interaction of hypnotizability, sex or hemisphere for the genu.

Rostral body corpus callosum region. Also contrary to the hypothesis that there would be differences in the anterior third of the CC, there was no significant difference in the volume of the rostral body between low and highly hypnotizable participants. Within groups, there were no significant main effects for sex or hemisphere. Finally, there was no significant interaction of hypnotizability, sex or hemisphere for the rostral body.

### Middle Third of Corpus Callosum

Anterior mid-body corpus callosum region. There were no significant differences in the volume of the anterior mid-body of the CC between low and highly hypnotizable participants. Also, there were no significant main effects for sex or hemisphere. Within groups, there were no significant main effects for sex or hemisphere. Finally, there was no significant interaction of hypnotizability, sex or hemisphere for the anterior mid-body.

Posterior mid-body corpus callosum region. While it was hypothesized that the posterior mid-body of the CC would be significantly smaller for highs than lows, no volume differences were observed between low and highly hypnotizable participants. Also, within groups, there were no significant main effects for sex or hemisphere. Finally, there was no significant interaction of hypnotizability, sex or hemisphere for the posterior mid-body.

## Posterior Third of Corpus Callosum

Isthmus corpus callosum region. There was a significant main effect for hypnotizability for the isthmus CC region. As illustrated in Figure 5.2, highly hypnotizable participants had a significantly larger isthmus volume than did low hypnotizable participants [Highs:  $M = 587.7$ ,  $SD = 88.0$ ; Lows:  $M = 511.8$ ,  $SD = 64.7$ ;  $F(1,7) = 6.590$ ,  $p < .04$ ]. Within groups, there were no significant main effects for sex or hemisphere. Finally, there was no significant interaction of hypnotizability, sex or hemisphere for the isthmus. The significant differences are summarized in the ANOVA source table for the isthmus in Table 5.2.

Splenium corpus callosum region. There were no significant differences in the volume of the splenium of the CC between low and highly hypnotizable participants. Also, within groups, there was no significant main effect for volume differences in sex. Also, there was no interaction between hypnotizability, sex or hemisphere for the splenium. However, as shown in Table 5.3, there was a significant hemisphere difference [ $F(1,7) = 6.271$ ,  $p < .041$ ] with the splenium volume of the right hemisphere ( $M = 266.10$ ,  $SD = 36.14$ ) larger than the left hemisphere ( $M = 257.20$ ,  $SD = 38.56$ ). The hemisphere difference is further analyzed and reported in a later exploratory post hoc section.

### Bulbosity of the Splenium.

Contrary to prior literature, there was no significant sex difference in the bulbosity of the splenium. Unexpectedly, there was an almost significant, but unpredicted, 3-way hypnotizability by sex by hemisphere interaction,  $F(2, 14) = 3.252$ ,  $p < .06$ . This interaction is further analyzed and reported in a later exploratory post hoc section.

### Medial Cortex Volume: Sex Differences

As expected, men had a significantly larger cortical volume in the medial cortex area than did women [Men:  $M = 49555.9$ ,  $SD = 1030.0$ , Women:  $M = 45442.1$ ,  $SD = 4283.8$ ;

$F(1,7) = 10.716, p < .014]$  (see Figure 5.5). It should be noted that this was the only significant sex difference observed in this study. As expected, there were no significant differences in hypnotizability, hemisphere, or interactions of variables for the medial cortex. Table 5.4 summarizes the ANOVA source table for the medial cortex.

#### Regression Analyses: Relationships of CC Regions, Forebrain, and Medial Cortex

As presented below, significant correlations were found between forebrain volume and the following CC regions: total CC, rostrum, isthmus, and splenium. No significant relationships were observed in the other CC regions. Quite interestingly, the significant relationships observed here are in the same CC regions in which hypnotic susceptibility volume differences were also observed (as presented previously). Thus, follow-up analyses in a later exploratory post hoc section will address potential differences within low and highly hypnotizable participants.

The relationships between the total medial CC (and CC regions) and the total medial cortex volumes were also assessed. No significant relationships were found: total CC ( $r = .29$ , adjusted  $R^2 = .03$ ), rostrum ( $r = .44$ , adjusted  $R^2 = .14$ ), isthmus ( $r = .37$ , adjusted  $R^2 = .09$ ), and splenium ( $r = .16$ , adjusted  $R^2 = .04$ ). Total medial cortex volume could contribute to the relationships between forebrain volume and the total medial CC volume (and CC regions). Therefore, partial correlations controlling for total medial cortex volume were performed for each significant or near-significant relationship between forebrain volume and medial CC volume (and CC regions) to determine the extent to which the medial cortex might be influencing the relationship of the CC and CC regions to the forebrain. Potential differences within low and highly hypnotizable participants are addressed in a post hoc exploratory section.

#### Total Medial Corpus Callosum

As hypothesized, there was a significantly positive relationship between CC and forebrain volumes ( $r = .58, p < .011$ ; adjusted  $R^2 = .30$ ). As expected, there was no significant

relationship between the total medial CC and medial cortex volume ( $r = .29$ ,  $p < .248$ ; adjusted  $R^2 = .03$ ). Partial correlation analysis of the total medial CC and forebrain volume controlling for medial cortex volume revealed an influence of the medial cortex on the relationship of the total medial CC and forebrain, but the correlation between the total medial CC and forebrain remained significant ( $r = .55$ ,  $p = .021$ ).

### Corpus Callosum Regions

#### Rostrum Corpus Callosum Region

As hypothesized, there was a significantly positive relationship between the rostrum and forebrain volumes ( $r = .59$ ,  $p < .011$ ; adjusted  $R^2 = .30$ ). The volume of the rostrum did not correlate significantly with the medial cortex volume ( $r = .44$ ,  $p < .069$ ; adjusted  $R^2 = .14$ ). Partial correlation analysis of the rostrum and forebrain volume controlling for medial cortex volume showed an influence of the medial cortex and resulted in a non-significant relationship between the rostrum and forebrain. However, there is an indicated trend toward a significant relationship ( $r = .44$ ,  $p = .081$ ).

#### Genu Corpus Callosum Region

There was no significant relationship between the genu and forebrain volume or between the genu and overall medial cortex volume.

#### Rostral Body Corpus Callosum Region

There was no significant relationship between the rostral body and forebrain volume or between the rostral body and overall medial cortex volume.

### Anterior Mid-body Corpus Callosum Region

There was no significant relationship between the anterior mid-body and forebrain volume or between the anterior mid-body and overall medial cortex volume.

### Posterior Mid-body Corpus Callosum Region

There was no significant relationship between the posterior mid-body and forebrain volume or between the posterior mid-body and overall medial cortex volume.

### Isthmus Corpus Callosum Region

There was a marginally significant correlation between the isthmus volume and the forebrain volume ( $r = .45$ ,  $p < .059$ ; adjusted  $R^2 = .15$ ). The volume of the isthmus did not correlate significantly with the medial cortex volume ( $r = .37$ ,  $p < .126$ ; adjusted  $R^2 = .09$ ). Partial correlation analysis of the isthmus and forebrain volumes, controlling for medial cortex volume, indicated an influence of the medial cortex and reduced the correlation further ( $r = .29$ ,  $p = .261$ ).

### Splenium Corpus Callosum Region

There was a significant correlation between the splenium volume and the forebrain volume ( $r = .56$ ,  $p < .017$ ; adjusted  $R^2 = .27$ ). The volume of the splenium did not correlate significantly with the overall cortex ( $r = .16$ ,  $p < .399$ ; adjusted  $R^2 = .04$ ). Partial correlation analysis of the splenium and forebrain volumes, controlling for medial cortex volume, resulted in a stronger relationship ( $r = .63$ ,  $p = .007$ ).

## Post Hoc Exploratory Analyses: Hemisphere Differences

Even though there were no significant interactions with hypnotizability and hemisphere in this study, various studies have reported hemisphere differences in low and highly hypnotizable individuals. Crawford et al. (1996) reported hemispheric asymmetries in EEG recordings (right greater than left) in the parietal region that involved high theta (5.5 – 7.45 Hz), high alpha (11.5 – 13.45 Hz), and beta activity (16.5 and 25 Hz) that was evident only in highly hypnotizable participants while participating in an experimental paradigm involving emotions. Various other studies using different paradigms have also reported greater EEG asymmetries and shifts in hemispheric dominance. MacLeod-Morgan and Lack (1982; see also De Pascalis & Palumbo, 1986) reported asymmetries in EEG activity in highly hypnotizable individuals, but not in low hypnotizable individuals, while performing tasks during waking and during hypnosis.

Other studies have reported EEG hemispheric asymmetries during rest and hypnotic suggestions (Sabourin et al., 1990) and painful stimulation (Crawford, 1990b; DePascalis & Perrone, 1996; Karlin et al., 1980). In response to cold pressor pain, Karlin et al. (1980) reported hemispheric shifts in total EEG power during hypnotic analgesia that were interpreted as greater overall right-hemisphere involvement at the bipolar parieto-occipital region. Also using cold pressor pain, Crawford (1990b) found only highly hypnotizable individuals exhibited hemispheric asymmetries of high theta when attending (left > right) and ignoring pain (right > left) in the anterior temporal region (Crawford, 1990b, 1994). Hemispheric shifts were previously interpreted as specific hemispheric dominance for hypnotizability (e.g., Gur & Gur, 1974) and more recently as task specific (Crawford & Gruzelier, 1992; Crawford et al., 1996; Jasiukaitis et al., 1997; MacLeod-Morgan, & Lack, 1982).

Crawford et al. (1996) proposed that the hemispheric shifts of higher theta power possibly reflects underlying hippocampal-cortical shifts of activity mediating neurophysiological influences of hypnotizability. These findings of hemispheric differences in EEG activity indicate possible underlying differences in hemisphere morphology between low and highly hypnotizable individuals in brain structures associated with attentional and

inhibitory processes. Therefore, post hoc exploratory analyses were performed on various areas of the CC to determine if there was a difference in hemispheric volume of low and highly hypnotizable participants that was obscured in the overall analyses.

### Morphological Differences in the Corpus Callosum

#### Anterior Third of Corpus Callosum

The rostrum was the only CC area in the anterior third of the CC to show significant differences in volume. The genu and rostral body volumes were not significantly different in hypnotizability, sex or hemisphere and there were no interactions between hypnotizability, sex or hemisphere.

Rostrum corpus callosum region. As illustrated in Figure 5.4, only highly hypnotizable participants had a significantly larger rostrum in the right hemisphere ( $M = 130.5$ ,  $SD = 46.7$ ) than in the left hemisphere ( $M = 102.9$ ,  $SD = 40.1$ ) [ $F(1,7) = 5.58$ ,  $p < .05$ ]. Low hypnotizable participants showed no significant asymmetry (Right hemisphere  $M = 68.2$ ,  $SD = 24.1$ ; Left hemisphere  $M = 61.0$ ,  $SD = 15.6$ ).

#### Middle Third of Corpus Callosum

There were no significant volume differences in the middle third of the CC. The anterior mid-body and the posterior mid-body volumes were not significantly different by hypnotizability, sex or hemisphere, and there were no significant interactions of hypnotizability, sex or hemisphere.

#### Posterior Third of Corpus Callosum

Isthmus corpus callosum region. As shown in Figure 5.5, further analyses revealed that highly hypnotizable participants had a significantly larger isthmus volume in the left

hemisphere (Lows  $M = 249.6$ ,  $SD = 39.2$ ; Highs  $M = 302.1$ ,  $SD = 57.0$ ) [ $F(1,7) = 5.364$ ,  $p < .017$ ] than did low hypnotizable participants. There was no significant difference in the right hemisphere (Lows  $M = 262.2$ ,  $SD = 38.1$ ; Highs  $M = 285.6$ ,  $SD = 41.0$ ) between low and highly hypnotizable participants. Finally, there was no significant difference in left versus right hemispheric volumes for either low or highly hypnotizable participants.

Splenium corpus callosum region. As illustrated in Figure 5.6, the splenium volume was significantly greater in the right than left hemispheres [ $F(1,7) = 6.271$ ,  $p < .041$ ]. The interaction between hypnotizability and hemisphere was not significant [ $F(1,7) = 3.456$ ,  $p < .105$ ], yet the figure suggests possible differences. Exploratory post-hoc analyses revealed that hemispheric asymmetry was only significant among the highs and not the lows. Specifically, the highs showed a significantly larger right hemisphere volume in the splenium (Left hemisphere:  $M = 455.8$ ,  $SD = 71.9$ , Right hemisphere:  $M = 481.4$ ,  $SD = 26.7$ ); [ $F(1,7) = 8.880$ ,  $p < .05$ ], whereas the lows did not (Left hemisphere:  $M = 469.6$ ,  $SD = 66.8$ , Right hemisphere:  $M = 473.4$ ,  $SD = 56.0$ ). This is worthy of further consideration in future research.

### Bulbosity of the Splenium

The mixed factorial ANOVA indicated there were no significant differences of hypnotizability, sex or hemisphere for the splenial bulbosity but there was an almost significant interaction ( $p < .06$ ) between hypnotizability, sex and hemisphere. Thus, further analyses were performed. Since the comparisons for the analyses were numerous, Bonferroni corrected  $t$ -tests were performed. As illustrated in Figure 5.7, various intriguing differences are indicated but only one was significant. There was a significant difference between the left and right hemisphere of low hypnotizable women [ $t_B(4) = 3.531$ ,  $p < .05$ ]. The bulbosity index for the left hemisphere ( $M = 5.9$ ,  $SD = 1.6$ ) indicated significantly more bulbosity than did the bulbosity index for the right hemisphere ( $M = 4.7$ ,  $SD = 2.0$ ) among these low hypnotizable women.

## Post Hoc Exploratory Analyses: Regression Analyses

Since analyses revealed hypnotizability differences for the CC and CC regions further analyses were performed to determine if hypnotizability influenced the relationships of the total medial CC and CC regions to the forebrain. The additional analyses revealed that only highly hypnotizable participants demonstrated significant correlations between forebrain volume and CC region volumes, whereas low hypnotizable participants did not show significant correlations. Partial correlations were not performed due to the reduced number of participants in each cell. Significance tests of betas were performed to compare slopes of regression lines between low and highly hypnotizable participants for each area analyzed.

### Total Medial Corpus Callosum

Further regression analyses revealed a robust correlation as shown in Figure 5.8, of CC and forebrain volumes for only highly hypnotizable participants ( $r = .72$ ,  $p < .043$ ; adjusted  $R^2 = .44$ ). The correlation of CC and forebrain volumes for low hypnotizable participants was not significant ( $r = .21$ ,  $p < .569$ ; adjusted  $R^2 = .08$ ). Significance tests of betas (Cohen & Cohen, 1983) show a significant difference in the slope of regression lines between low and highly hypnotizable participants [ $t(14) = 6.115$ ,  $p < .001$ ].

### Corpus Callosum Regions

#### Rostrum Corpus Callosum Region

Further regression analyses revealed a significant correlation of rostrum and forebrain volumes, as shown in Figure 5.8, for only highly hypnotizable participants ( $r = .67$ ,  $p < .041$ ; adjusted  $R^2 = .35$ ). The correlation of rostrum and forebrain volumes for low hypnotizable participants was not significant ( $r = .27$ ,  $p < .442$ ; adjusted  $R^2 = .04$ ). Significance tests of betas (Cohen & Cohen, 1983) show a significant difference in the slope of regression lines

between low and highly hypnotizable participants [ $t(14) = 13.933, p < .001$ ].

### Isthmus Corpus Callosum Region

Since significant differences were revealed for hypnotizability in the overall CC and rostrum, further regression analyses were performed for the isthmus. The additional analyses revealed a robust correlation, as shown in Figure 5.9, for highly hypnotizable participants ( $r = .82, p < .013$ ; adjusted  $R^2 = .62$ ) but not for low hypnotizable participants ( $r = .29, p < .419$ ; adjusted  $R^2 = -.03$ ). Significance tests of betas (Cohen & Cohen, 1983) show a significant difference in the slope of regression lines between low and highly hypnotizable participants [ $t(14) = 11.859, p < .001$ ].

### Splenium Corpus Callosum Region

Further regression analyses revealed a robust correlation with splenium volume, as shown in Figure 5.10, for only highly hypnotizable participants ( $r = .74, p < .038$ ; adjusted  $R^2 = .46$ ) but not for low hypnotizable participants ( $r = .41, p < .242$ ; adjusted  $R^2 = .06$ ). Significance tests of betas (Cohen & Cohen, 1983) show a significant difference in the slope of regression lines between low and highly hypnotizable participants [ $t(14) = 6.293, p < .001$ ].

Table 5.1

Rostrum Volume: ANOVA Source Table.

Source	SS	df	MS	F	P
Hypnotizability Level	24118.249	1	24118.249	12.903	.009
Error (Hypnotizability Level)	13084.265	7	1869.181		
Sex	2612.327	1	2612.327	1.197	.310
Sex X Hypnotizability Level	106.607	1	106.607	.049	.831
Error (Sex)	15271.380	7	2181.626		
Hemisphere	2699.907	1	2699.907	5.575	.050
Hemisphere X Hypnotizability Level	929.907	1	929.907	1.92	.208
Error (Hemisphere)	3390.124	7	484.303		
Sex X Hemisphere	617.438	1	617.438	2.242	.178
Sex X Hemisphere X Hypnotizability Level	912.938	1	912.938	3.315	.111
Error (Sex X Hemisphere)	1927.905	7	275.415		

Table 5.2

Isthmus Volume: ANOVA Source Table.

Source	SS	df	MS	F	P
Hypnotizability Level	12813.188	1	12813.188	6.590	.037
Error (Hypnotizability Level)	13610.172	7	1944.310		
Sex	1606.976	1	1606.976	.559	.479
Sex X Hypnotizability Level	11387.185	1	11387.185	3.959	.087
Error (Sex)	20133.947	7	2876.278		
Hemisphere	32.195	1	32.195	.022	.887
Hemisphere X Hypnotizability Level	1884.226	1	1884.226	1.261	.298
Error (Hemisphere)	10458.629	7	1494.090		
Sex X Hemisphere	18.288	1	18.288	.026	.877
Sex X Hemisphere X Hypnotizability Level	20.757	1	20.757	.029	.869
Error (Sex X Hemisphere)	4933.789	7	704.827		

Table 5.3

Splenium Volume: ANOVA Source Table.

Source	SS	df	MS	F	P
Hypnotizability Level	72.200	1	72.200	.020	.892
Error (Hypnotizability Level)	25332.543	7	3618.935		
Sex	14196.456	1	14196.456	1.209	.308
Sex X Hypnotizability Level	20072.448	1	20072.448	1.709	.232
Error (Sex)	82193.663	7	11741.952		
Hemisphere	1917.861	1	1917.861	6.271	.041
Hemisphere X Hypnotizability Level	1057.058	1	1057.058	3.456	.105
Error (Hemisphere)	2140.805	7	305.829		
Sex X Hemisphere	497.503	1	497.503	1.021	.346
Sex X Hemisphere X Hypnotizability Level	35.113	1	35.113	.072	.796
Error (Sex X Hemisphere)	3410.312	7	487.187		

Table 5.4

Medial Cortex Volume: ANOVA Source Table.

Source	SS	df	MS	F	P
Hypnotizability Level	7700101.00	1	7700101.00	1.210	.308
Error (Hypnotizability Level)	44540211.0	7	6362887.30		
Sex	35651429.0	1	35651429.0	10.716	.014
Sex X Hypnotizability Level	2117472.17	1	2117472.17	.636	.451
Error (Sex)	23288282.5	7	3326897.49		
Hemisphere	231452.991	1	231452.991	.677	.438
Hemisphere X Hypnotizability Level	519475.086	1	519475.086	1.519	.258
Error (Hemisphere)	2393392.25	7	341913.179		
Sex X Hemisphere	43224.078	1	43224.078	.135	.724
Sex X Hemisphere X Hypnotizability Level	560128.818	1	560128.818	1.751	.227
Error (Sex X Hemisphere)	2239872.24	7	319981.749		

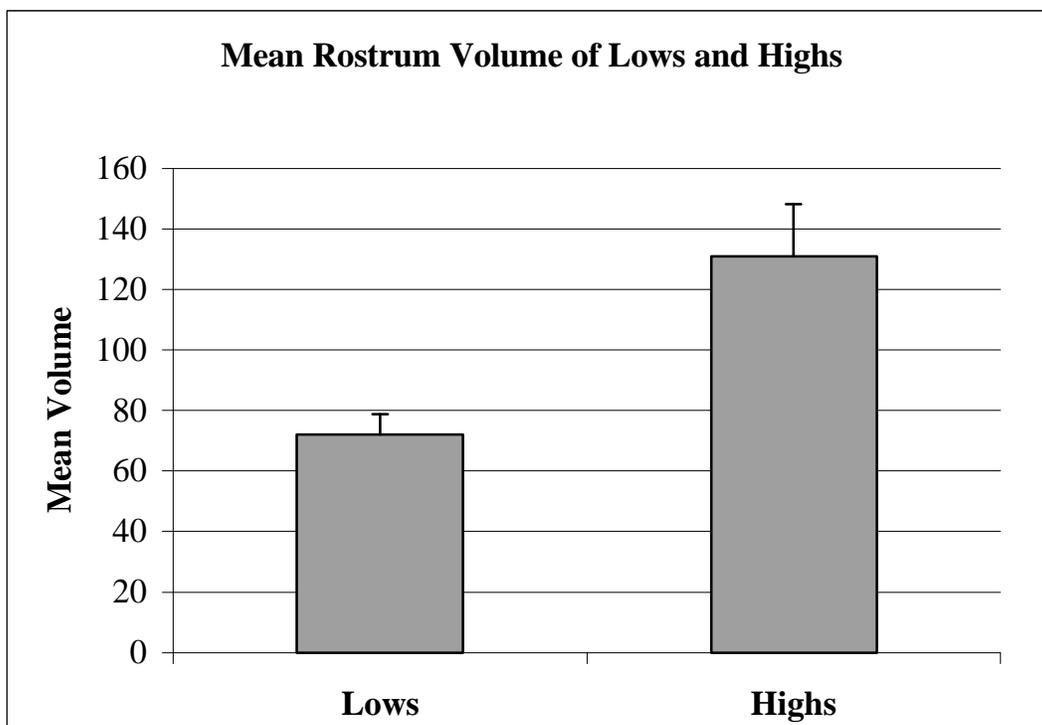


Figure 5.1

Mean Rostrum Volume of Low and High Hypnotizable Participants

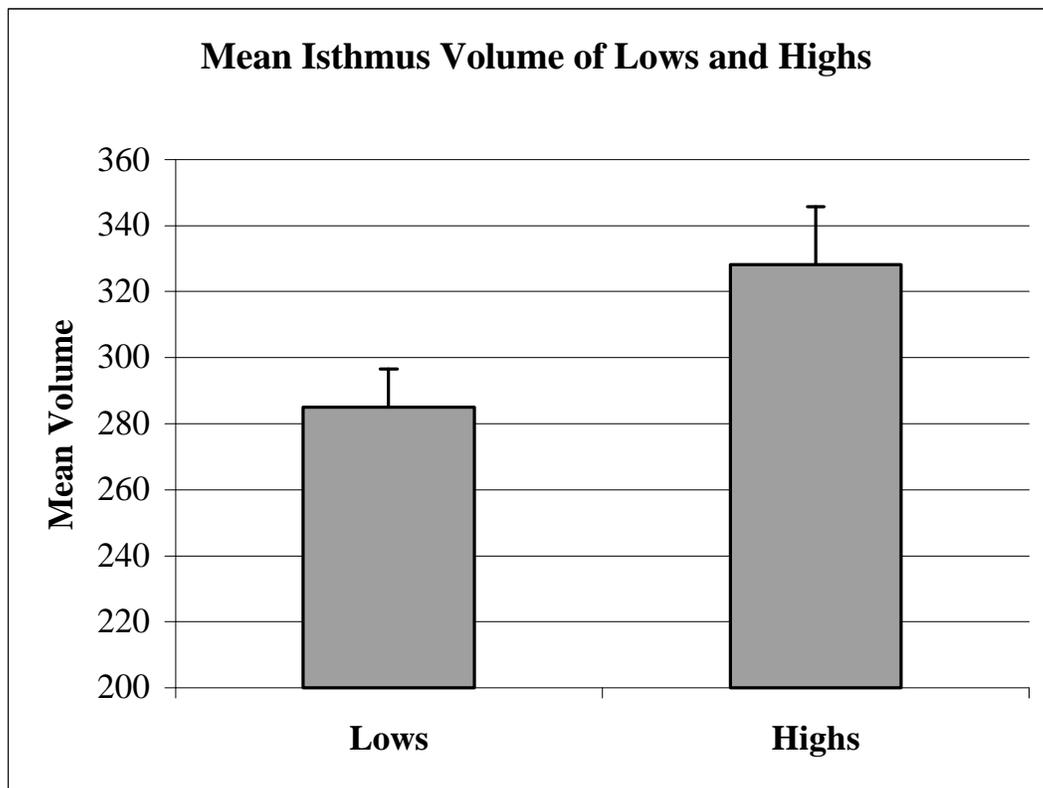


Figure 5.2

Mean Isthmus Volume of Low and Highly Hypnotizable Participants

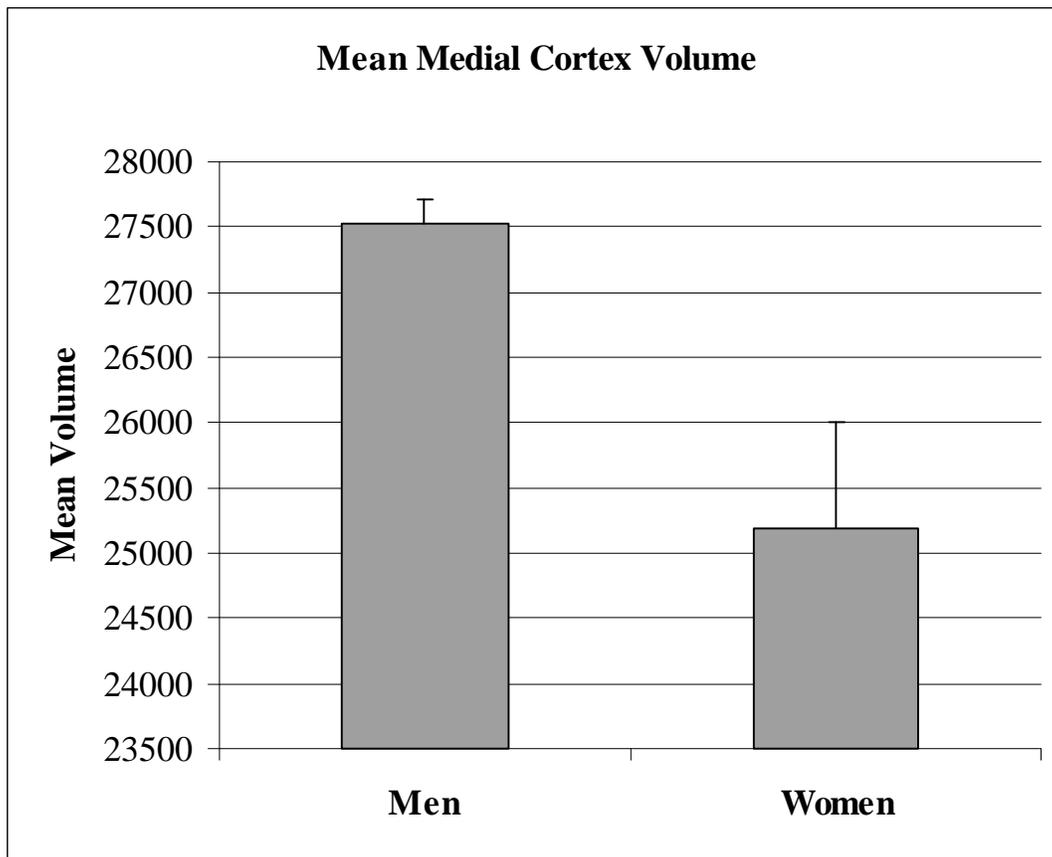


Figure 5.3  
Mean Medial Cortex Volume of Men and Women

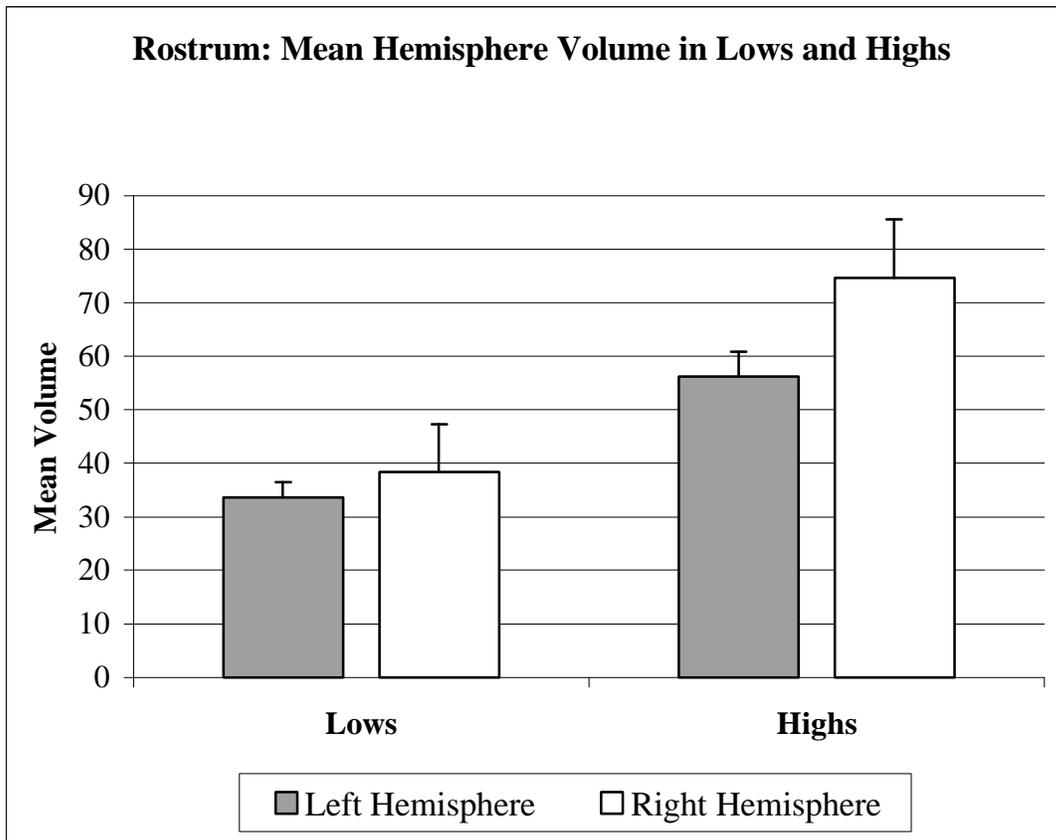


Figure 5.4  
Mean Rostrum Volume  
in Left and Right Hemispheres of Low and High Hypnotizable Participants

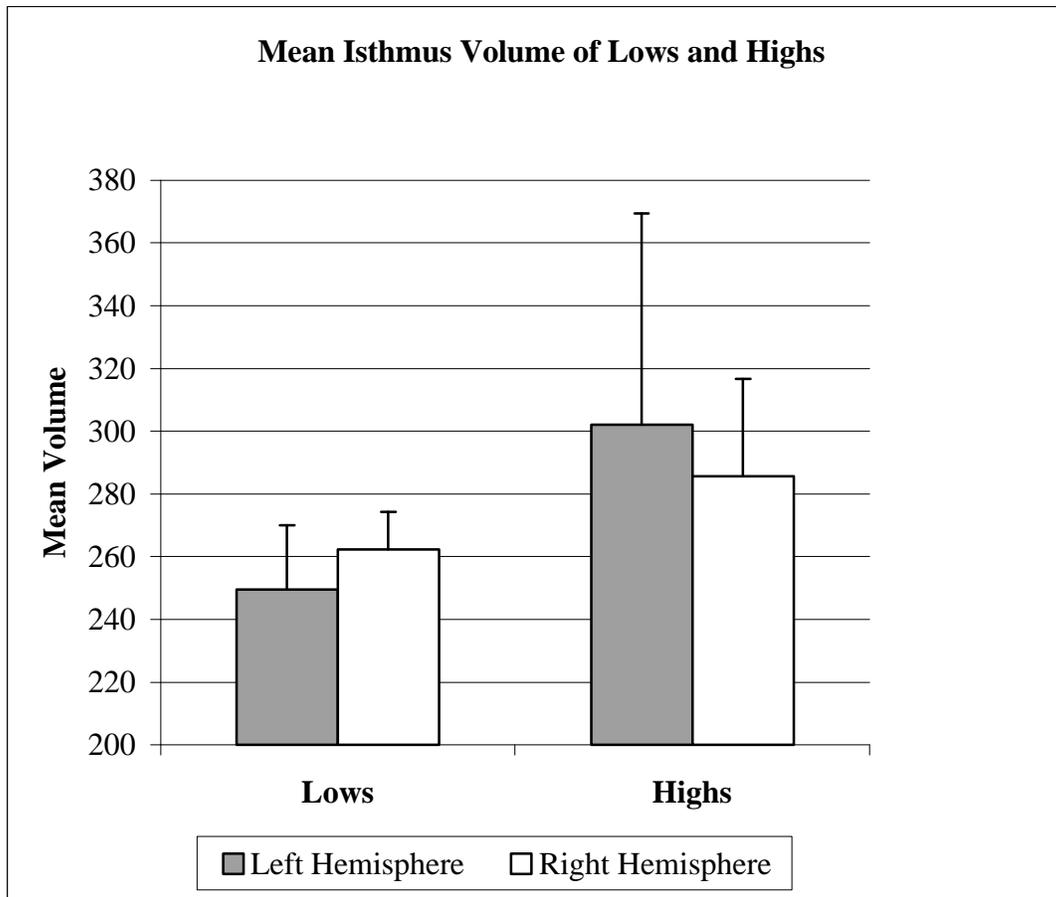


Figure 5.5

Mean Isthmus Volume

in Left and Right Hemispheres of Low and High Hypnotizable Participants

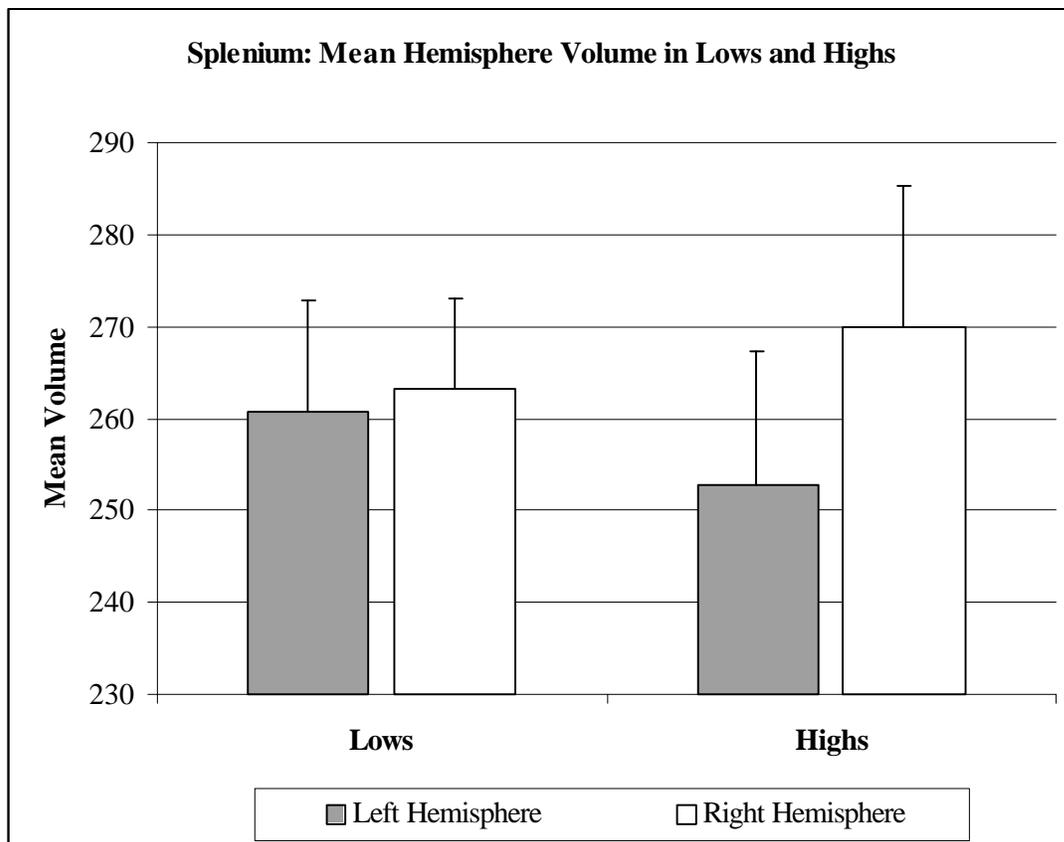


Figure 5.6  
Mean Splenum Volume  
in Left and Right Hemispheres of Low and High Hypnotizable Participants

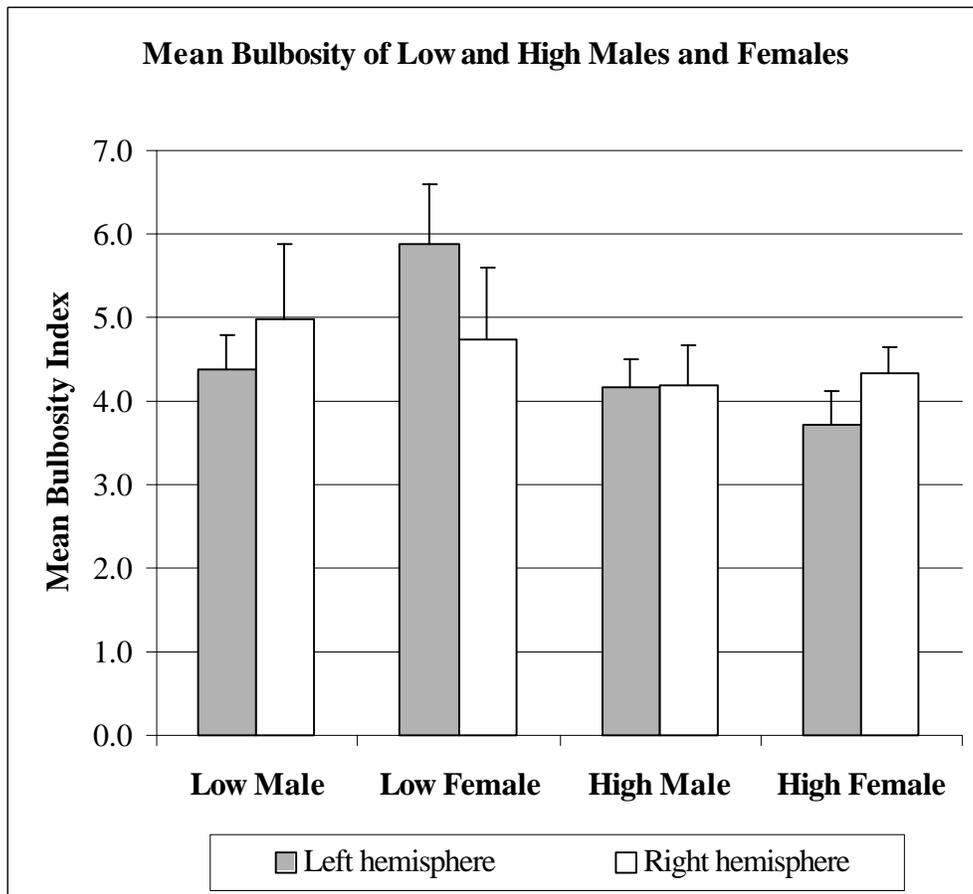


Figure 5.7

Mean Splenium Bulbosity in Left and Right Hemispheres of Low and High Hypnotizables

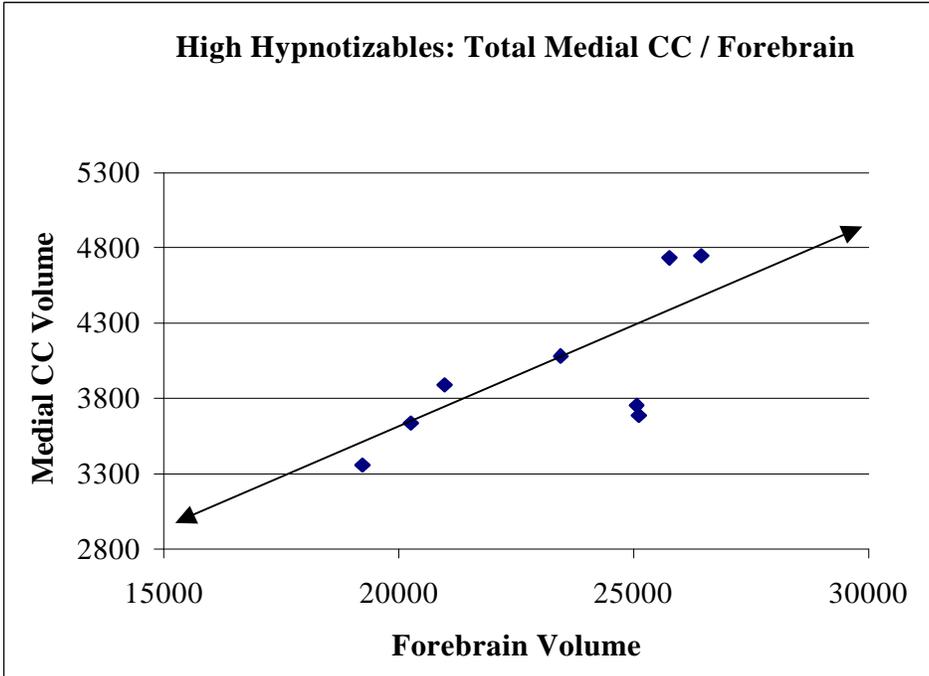
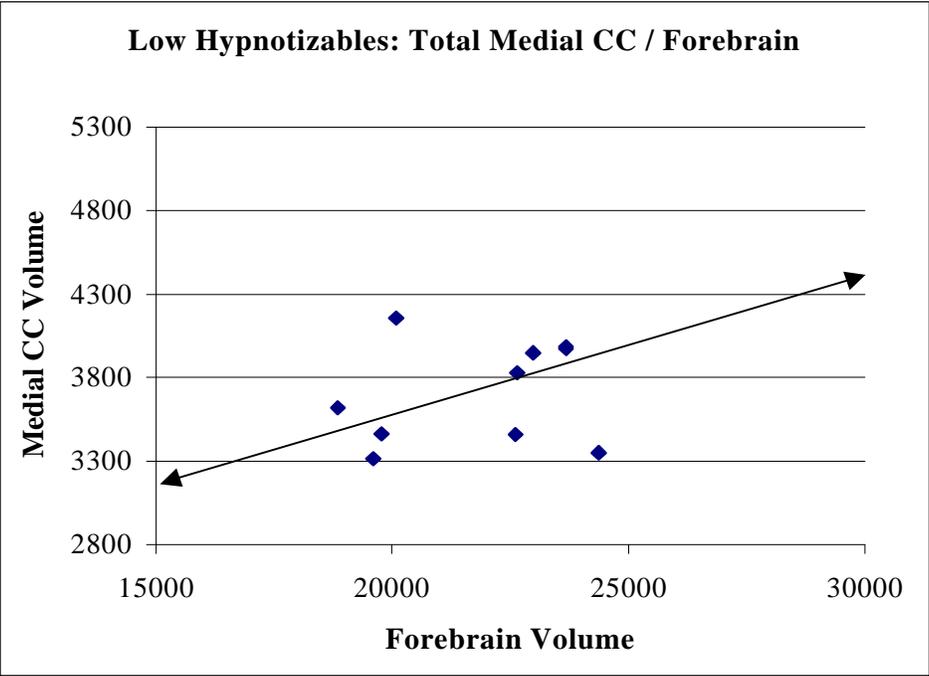


Figure 5.8

Relationship of Total Medial Corpus Callosum Volume to Medial Forebrain Volume

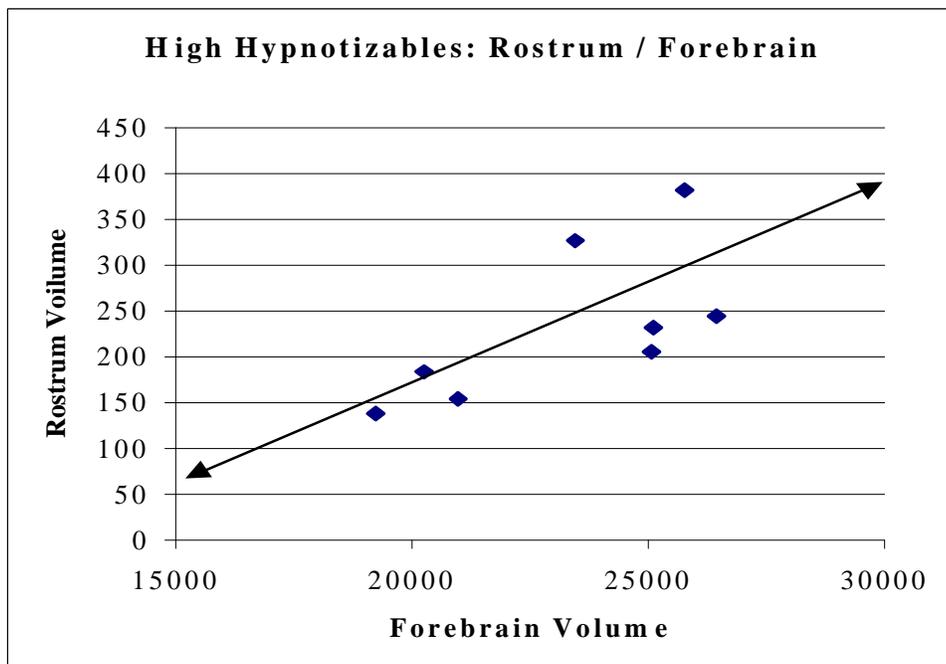
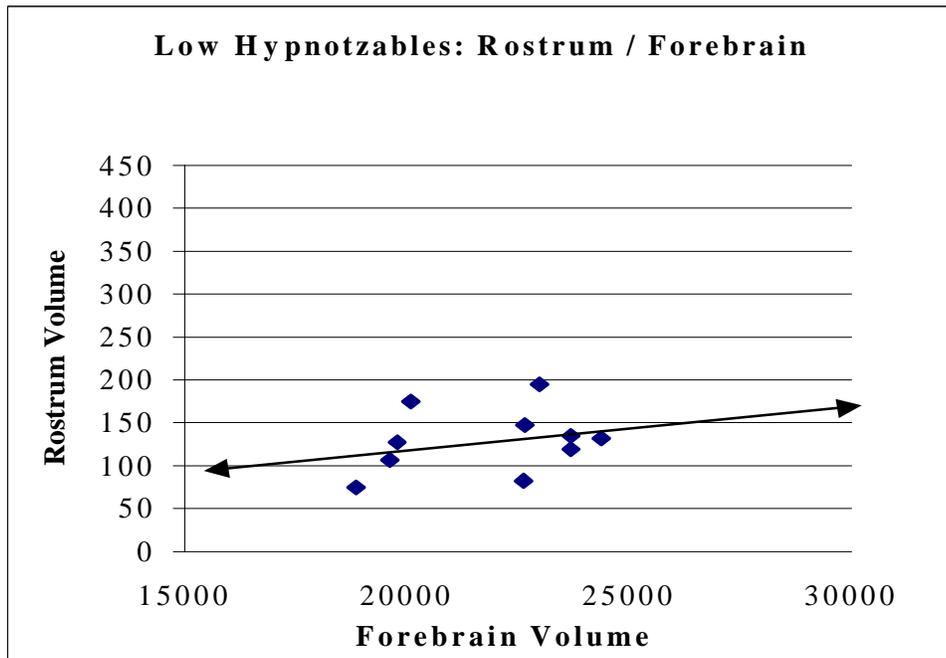


Figure 5.9

Relationship of Rostrum Volume to Medial Forebrain Volume

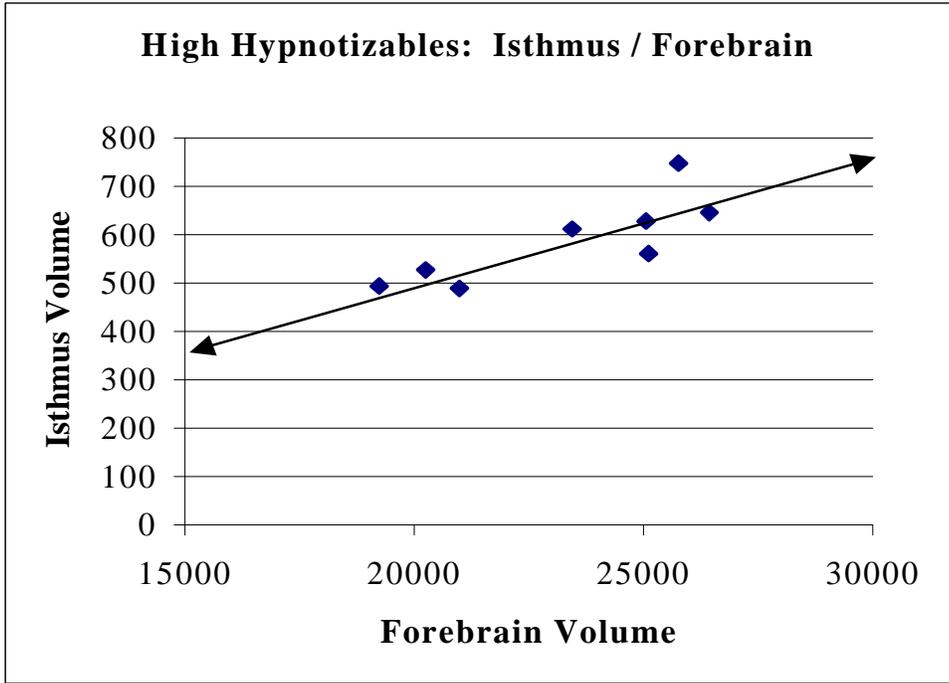
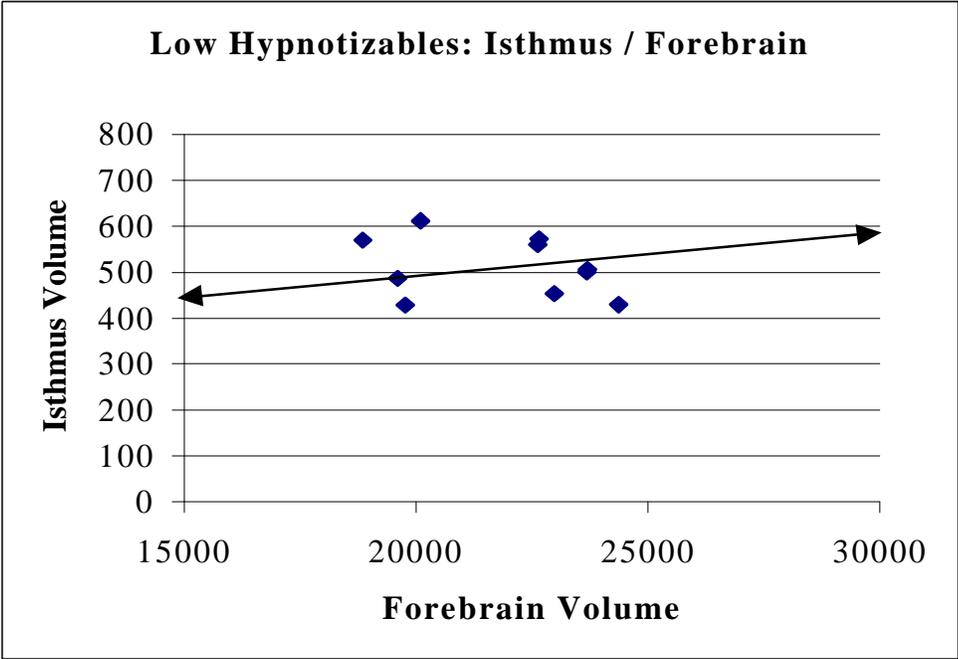


Figure 5.10

Relationship of Isthmus Volume to Medial Forebrain Volume

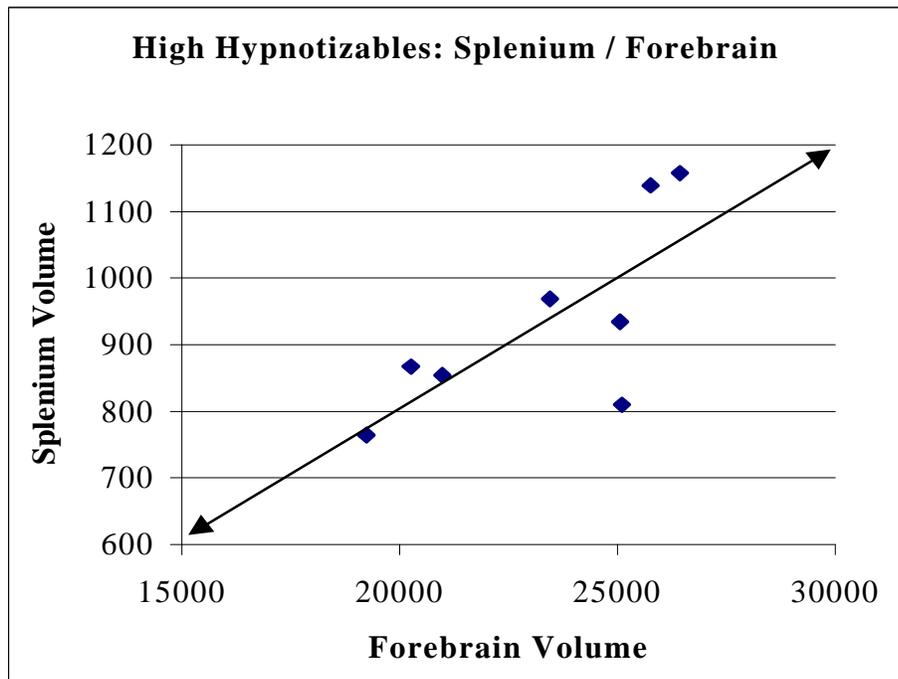
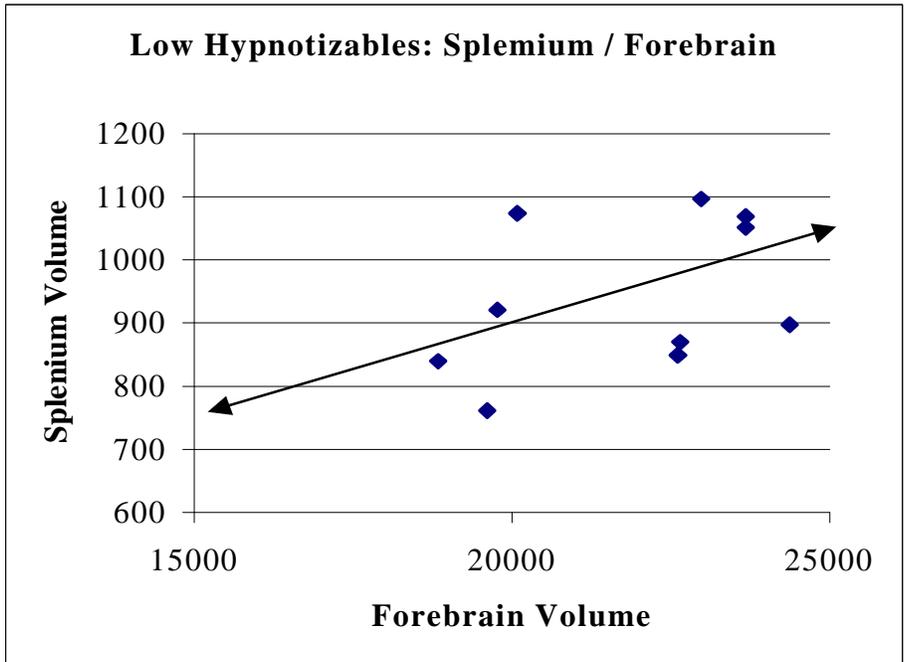


Figure 5.11

Relationship of Splenium Volume to Medial Forebrain Volume

## CHAPTER 6

### DISCUSSION

This is the first morphological study to determine that there are significant differences in brain morphology between highly hypnotizable and low hypnotizable young adults who, respectively, could and could not eliminate the perception of pain. Of the four regions studied, the primary brain region to be implicated was the corpus callosum (CC). As hypothesized, highly hypnotizable participants had a significantly larger anterior CC rostrum than did low hypnotizable participants. Furthermore, highly hypnotizable participants had a significantly larger posterior isthmus. These findings are especially salient for understanding individual differences in the involvement of anterior frontal and posterior regions involved in attentional and inhibitory processing systems. If a larger CC reflects more effective neural processing, then these data support prior behavioral and electrophysiological data that show that highly hypnotizable individuals have significantly more effective attentional and inhibitory processing abilities than low hypnotizables (e.g., for review, see Crawford 1994). Whether these differences are due to developmental or hereditary influences are unknown as of yet and require further research, but they do provide some support to prior research (Lichtenberg, Bachner-Melman, Gritsenko, & Ebstein, under review; Morgan, 1973) that suggests there is a heritability factor involved in hypnotizability.

#### Anterior Corpus Callosum

#### Rostrum Corpus Callosum Region

#### Volume Analyses

As expected, and in partial support of the first hypothesis that the anterior third of the CC would be larger in highly hypnotizable participants, the rostrum was significantly larger in highly hypnotizable participants than in low hypnotizable participants. These findings were expected since the rostrum contains neurons that project to the orbitofrontal region of the

cortex (BA 11, 12 & 13). No morphological differences were observed in the genu and rostral body, two anterior CC regions that project to, respectively, the dorsolateral and ventrolateral frontal regions of the cortex.

The prefrontal cortex is divided into three primary regions based on projections from the mediodorsal nucleus of the thalamus. The mediodorsal nucleus of the thalamus projects to the orbitofrontal cortex and to areas of the anterior cingulate (Fuster, 1989). Paralleling the projections of the mediodorsal nucleus of the thalamus, the rostrum of the CC also projects to the orbitofrontal cortex and the anterior cingulate. The anterior cingulate is also involved in attentional and inhibitory processing (Posner, 1995; Vogt et al., 1992), active selective attention (Kropotov, et al, 1995) and emotional processing (Lane et al., 1998). Furthermore, the orbitofrontal cortex is interconnected with the limbic system, and therefore is also associated with emotion (Kupfermann, 1991), attentional processes (Posner, 1995), and inhibitory processes (Crawford, Gur, et al., 1993). Based primarily on neuropsychological investigations, Rolls (1998) suggested that the orbitofrontal cortex is associated with executive functions of influencing behavioral response to reinforcing stimuli and is particularly involved in reward or punishment association learning. Given that pain may be considered a punishment, it is of particular interest that the rostral CC area, that connect particularly to the orbitofrontal region, discriminated between those who can and cannot inhibit pain. Crawford, Gur et al. (1993) found increased orbitofrontal CBF activation only in highly hypnotizable individuals during hypnotic analgesia. Based upon PET studies that showed an increase of activity during the performance of willed actions, they interpreted these data to reflect increased inhibitory effort by the supervisory attentional system (Shallice, 1988) in the successful elimination of incoming noxious stimuli from conscious perception. Furthermore, Kropotov et al. (1997) recorded a significant reduction of the P140-160 component of the somatosensory ERP from the anterior cingulate during hypnotic analgesia. This supports other findings that the anterior cingulate is involved in pain processing (e.g., for review, see Devinsky, Morrell, & Vogt, 1995) and shows significant reductions of activation during hypnotic analgesia in fMRI (Crawford, Horton, Harrington, et al., 1998) and PET (Rainville et al., 1997, 1999) studies.

Prior research suggests a relationship between CC efficiency and attentional processing abilities. For instance, Jäncke et al. (1997) found positive relationships between CC and forebrain volumes and interpreted their data as being suggestive of a relationship between CC efficiency and attentional processes. In a study of individual differences in vigilance performance and incongruent/congruent simultaneous movements of the left and right hands, Rueckert and Levy (1996) concluded that the CC is involved in the ability to sustain attention over a long period of time.

Providing further support to the observed rostrum differences being associated with attentional and inhibitory differences are a series of studies (reviewed in greater depth in the introduction) that support the proposal that highly hypnotizable individuals have greater attentional and inhibitory abilities that are reflected at both behavioral (e.g., Crawford, Knebel, Kaplan, et al., 1998; Spiegel, et al., 1989; Zachariae & Bjerring, 1994; for review, see E. R. Hilgard & J. R. Hilgard, 1994) and physiological levels (e.g., Crawford, 1994a, 1994b; Crawford, Gur, et al., 1993; Crawford, Knebel & Vendemia, 1998; Crawford, Knebel, Vendemia & Horton, in press; Crawford & Gruzelier, 1992; Crawford, Horton, Harrington, et al., 1998; Gruzelier & Warren, 1993).

Several somatosensory (Crawford, Knebel, Xie, et al., under review; Crawford, Knebel, Kaplan, et al., 1998; Horton et al., 1998; McClain-Furmanski et al., 1999) and auditory (Lamas & Crawford, 1997, 1998; Lamas, Crawford, & Vendemia, under review) ERP studies have found certain ERP component latencies, as early as 50 msec, to be faster in high than low hypnotizables. These researchers concluded that their data suggest that highly hypnotizable individuals demonstrate faster neural processing than low hypnotizables. Furthermore, Crawford, Knebel, Xie, et al., (under review) found somatosensory ERP latency differences that suggest neural processing speed differences across the hemispheres in healthy individuals who were low and highly hypnotizable. Highly hypnotizable participants had significantly faster interhemispheric transmission time (IHTT) as determined by differences in certain ERP component latencies in each hemisphere across several electrode sites in the frontal and parietal areas. Thus, these data suggest more effective (faster) neural processing, and possibly IHTT differences, among highly hypnotizable individuals. Thus, it is logical that morphological differences in the CC would be reflected by a larger rostrum volume in

highly hypnotizable participants, possibly more so among those who can completely eliminate or reduce the perception of pain.

A significantly larger rostrum in highly hypnotizable participants may be associated with increased neural processing speed that facilitates excitatory or inhibitory process via the CC. Thus, these findings support the more recent approaches of Banich (1995a, 1995b, 1998) and Chiarello (1995) that consider the duality of function in the CC with excitatory and inhibitory processing. It is also compatible with the findings of Karbe, Herholz, Halber and Heiss (1998) who, in a multimodal imaging study using MRI and PET found an inverse correlation of activity in the cortex and CC. As cortical activity increased CC activity decreased, leading Karbe and colleagues to suggest the influence of precallosoal inhibition of transcallosal activity as facilitating asymmetrical processing.

Some theoretically important rostral hemispheric differences were observed. Overall, the rostrum in the right hemisphere was significantly larger than the rostrum in the left hemisphere. Further post hoc exploratory analyses revealed this hemispheric difference was only found in the highly hypnotizable participants while there was no significant difference in the low hypnotizable participants (Figure 5.4). This is of particular theoretical importance as it is consistent with prior studies that reported observing greater EEG hemispheric asymmetries and shifts in hemispheric dominance among highly hypnotizable than low hypnotizable individuals (e.g. Crawford, 1990b; Crawford et al., 1996; De Pascalis & Palumbo, 1986; DePascalis & Perrone, 1996; Karlin et al., 1980; MacLeod-Morgan & Lack, 1982; Sabourin et al., 1990).

Hemispheric asymmetry in highly hypnotizable individuals has been interpreted as task specific (Crawford & Gruzelier, 1992; Crawford et al., 1996; Jasiukaitis et al., 1997; MacLeod-Morgan, & Lack, 1982). Thus, the ability of highly hypnotizable individuals to inhibit perception of pain may be reflective of task specific hemisphere specificity (Crawford, 1990a) and may be associated with morphological differences of brain structures as indicated by a larger rostrum volume in the right hemisphere of the highly hypnotizable participants of this study.

If low hypnotizables have a smaller rostral CC that is associated with decreased sustained attention and increased distractibility, one should observe similar size differences in clinical

populations that present attentional problems. The most consistent findings in studies of individuals with attention deficit disorders are evidence of ineffective or dysfunctional prefrontal-striatal systems involving loss of normal right > left asymmetry of caudate, reduced right hemisphere globus pallidus and smaller right anterior frontal brain regions (Castellanos et al., 1996). Other researchers have reported decreased volume size of several anterior regions of the brain. Specifically, significantly smaller rostrum and rostral body volumes have been observed in individuals diagnosed with ADHD as compared to controls (Baumgardner, et al., 1996; Giedd et al., 1994). Of further interest are two recent genetic studies (Eisenberg et al., in press; Lichtenberg, et al., under review), discussed in greater detail in a subsequent section, the ADHD and low hypnotizability correlate similarly with the presence of the gene that codes for the activity of catechol-O-methyltransferase (COMT), an enzyme involved with dopaminergic and noradrenergic (but not serotonergic) metabolism. Taken together, these studies along with the present one suggest the possibility of an attention continuum from attentional deficits (ADHD and to a lesser degree low hypnotizables), with lesser morphological volumes, to more effective attentional processes (highly hypnotizable individuals), with greater morphological volumes. Yet, it should be noted that there are other dimensions of ADHD/ADD that do not appear to overlap with low hypnotizability characteristics, and thus may temper this suggested relationship. This possibility is certainly worthy of further investigation. In general, these rostrum data lend support to the neuropsychophysiological model proposed by Crawford and her colleagues (e.g., Crawford, 1989, 1990, 1994; Crawford & Gruzelier, 1992) that suggested the involvement of a more effective anterior frontolimbic system in highly hypnotizable individuals.

### Regression Analyses

Regression analysis of rostrum volume with forebrain volume initially was positive but when partial correlations were used to control for the influence of overall total medial cortex volume, the correlation of rostrum volume with forebrain volume was nonsignificant but indicated a trend toward a significant relationship. Thus, post hoc exploratory analyses revealed unexpected differences between low and highly hypnotizable individuals. There was

a significant relationship of rostrum volume with forebrain volume for highly hypnotizable participants only. Using Cohen and Cohen's (1983) method of beta comparison, a highly significant difference between the regression slopes of low and highly hypnotizable participants was observed.

As noted earlier, the rostrum contains projections to the orbitofrontal cortex and anterior cingulate that are involved in attentional and inhibitory processing (Posner, 1995; Vogt et al., 1992). The increased relationship between rostrum volume and forebrain volume may be influential in the establishment of more effective neural processing demonstrated by highly hypnotizable individuals (Crawford, Horton, & Lamas, 1998; Horton et al., 1998). Furthermore, that there were significant relationships observed only among highly hypnotizable individuals and not low hypnotizables suggest potential differences in the development of the connections between the CC and frontal region in these to hypnotic level groups. It suggests that future research should examine relationships between the CC and frontal regions in individuals differing in attentional and inhibitory abilities.

## Posterior Corpus Callosum

### Isthmus Corpus Callosum Region

#### Volume Analyses

The volume of the isthmus was significantly larger among highly hypnotizable participants than among low hypnotizable participants. Further post hoc exploratory analyses revealed this significant difference was only observed in the left hemisphere (Figure 5.5) The isthmus contains projections to tertiary association areas (BA 5 & 7) in the parietal lobes that are involved in the integration of information from different modalities. Brodmann area 5 has connections to primary somatosensory cortex (BA 1 & 2), motor cortex (BA 4) and superior temporal cortex (BA 22). Brodmann area 7 has connections to primary somatosensory cortex (BA 1 & 2) and is connected to BA 7 (Talairach & Tournoux, 1988). The greater isthmus volume found in the highly hypnotizable individuals may reflect a more effective posterior

attention system (Posner, 1995), in addition to the previously discussed more effective anterior system, to be associated with hypnotizability.

The data suggests that individual differences in the abilities to effectively attend to or disattend to a stimulus while integrating information from different modalities may be related to rostrum volume (see further discussion in the following section on the splenium). Such a proposal is supported by the findings that participants diagnosed with ADHD have a significantly smaller isthmus region of the CC than controls (Filipek et al., 1997).

### Regression Analyses

There was a marginally significant positive correlation between isthmus and forebrain volumes. Just as was found for the rostrum (see above), post hoc exploratory analyses revealed unexpected differences between low and highly hypnotizable individuals. There was a significant relationship between isthmus volume and forebrain volume found only for the highly hypnotizable participants. Using Cohen and Cohen's (1983) method of beta comparison, a highly significant difference between the regression slopes of low and highly hypnotizable participants was observed.

### Splenium Corpus Callosum Region

#### Volume Analyses

While there were no overall splenium volume differences between hypnotic level groups, exploratory post-hoc analyses of the splenium revealed significant hemispheric differences present among the highly hypnotizable participants but not among the low hypnotizable participants. The highly hypnotizable participants had a significantly larger splenium in the right than left hemisphere.

The findings of larger volumes of the isthmus and splenium in highly hypnotizable individuals support the concept of a parietal attention system, that may also involve parietotemporal activity, associated with the modulation of emotion (Crawford et al., 1996;

Heller, 1993) and reaction time (Heller, 1993); Levine, Yen, & Kim, 1992). In general, the isthmus and splenium both have projections into parietal and temporal areas. Therefore, it may be suggested that the significant increased volume in the isthmus and splenium in the posterior regions of the CC in highly hypnotizable participants may facilitate more effective neural processing and more effective use of posterior attentional systems. Subsequently, the morphological differences in posterior regions of the CC may be related to the ability of highly hypnotizable individuals to more effectively allocate attention towards and away from the sensory aspects of pain.

Furthermore, individual differences in reaction time may be related to parietal dynamic hemispheric differences. Levy et al. (1983) proposed that the large variability in hemispheric activity may be due, in part, to individual variation in patterns of asymmetrical parietotemporal hemispheric activity. Right parietal lesions produce slowing of reaction times (e.g., Benton, 1986) and “non-brain-damaged individuals who exhibit higher right-hemisphere activity as inferred from behavioral measures showed faster reaction time when orienting toward visual stimuli” (Levine, et al., 1992, cited in Heller, 1993, pp. 480).

Prior behavioral research showed that highly hypnotizable individuals exhibited faster responses than low hypnotizable individuals when engaged in complex decision making tasks such as determining an emotion portrayed by faces presented to either the right or left visual fields (Crawford et al., 1995). They also showed faster responses when identifying differences between pictures presented sequentially (Crawford & Allen, 1983) or visuo-spatial stimuli (Mészáros et al., 1989). Also, in a study of positive and negative emotional states, Crawford et al. (1996) found that highly hypnotizable individuals exhibited significantly greater high theta power in the right parietal region of the cortex. They interpreted this as being indicative of parietotemporal activity in the modulation of emotional states, as proposed by Heller (1993).

Similar to the rostrum data, the finding of larger isthmus and splenium in highly hypnotizable participants suggests that individual differences in the abilities to effectively attend or disattend to a stimulus while integrating information from different modalities may be related to splenium volume size. Supportive of such a proposal is the findings that participants diagnosed with ADHD have a significantly smaller splenium region of the CC

than controls. Hynd et al. (1991) reported smaller areas of the CC in ADHD children; these included the genu, splenium and area just anterior to the splenium (posterior portion of the isthmus). A study using MRI and shape analysis by Semrud-Clikeman et al. (1994) supported Hynd et al. (1991). They also found smaller CC regions in the posterior portion of the CC with the splenium accounting for the majority of the differences, but they did not find any significant differences in the anterior portion of the CC. The degree to which there are similar morphological similarities between low hypnotizables and individuals with ADHD is worthy of further investigation. Our present sample of low hypnotizables did not report any diagnoses for ADHD or other learning disorders. Yet, we know that like individuals with attention deficit disorder, low hypnotizables report greater distractibility to environmental stimuli and less sustained focused attention than highly hypnotizable individuals (e.g., Crawford et al., 1993; Lyons & Crawford, 1997; Tellegen & Atkinson, 1973). As noted earlier, there are other dimensions on which they differ and thus one must be cautious in such comparisons until further research is carried out.

### Regression Analyses

Regression analysis of splenium volume with forebrain volume was positive and remained significant when partial correlations were used to control for the influence of overall total medial cortex volume. Post hoc exploratory analyses were performed and revealed that a significantly positive relationship between splenium volume and forebrain volume was only observed among highly hypnotizable participants. Analyses of regression slopes by Cohen and Cohen's (1983) method of beta comparison, revealed a significant difference between the regression slopes of low and highly hypnotizable participants.

### Bulbosity Analyses

This study did not support prior findings of sex differences in the bulbosity of the splenium (e.g. Davatzikos & Resnick, 1998). It did find an interaction between sex and hypnotizability for the bulbosity index: A more bulbous splenium was present in the right

hemisphere of low hypnotizable women. The bulbosity index is based on Clarke's (1989) formula; it uses a combination of maximum splenial width and minimum presplenial thickness in the isthmus to determine a bulbosity index. Therefore, any findings regarding bulbosity should indicate a reciprocal and inverse finding regarding the isthmus with respect to hypnotizability, sex or hemisphere differences. Thus, there was an inverse relationship of bulbosity and isthmus volume for low hypnotizable women. The low hypnotizable women had a significant bulbosity index in the left hemisphere and an indication of less volume of the isthmus. However, after Bonferroni correction, there was not a significant difference in the volume of the isthmus in the left hemisphere.

### Middle Third of Corpus Callosum

#### Posterior Mid-body Corpus Callosum Region

Contrary to what was proposed, there was no significant difference in CC posterior mid-body volume between low and highly hypnotizable participants. There also were no significant relationships between the posterior mid-body and forebrain volumes.

#### Relationship Between the Total Corpus Callosum and Forebrain Volumes

As predicted, there was a positive relationship between the total CC and specific regions of the CC with forebrain volume. The regions of the CC that were correlated with forebrain volume were the rostrum, isthmus, and splenium. All of the CC regions that correlated with forebrain volume were the CC regions that were significantly larger in highly hypnotizable participants. These findings are similar to and support the findings of Jäncke et al. (1997) that an increased CC size (total CC, anterior third, and isthmus of the CC) correlated with an increased forebrain volume. These data support the proposal that the anterior and posterior attentional and inhibitory systems are more effective in highly hypnotizable individuals (e.g., Crawford, 1994a, 1994b; Crawford & Gruzelier, 1992; Schacter, 1977).

As reported by Pribram (1991), it is generally known that there are strong cortico-cortical connections between the parietal and ventro-frontal areas of the brain. The correlation between certain CC regions and forebrain volume showed a significant main effect for hypnotizability. This suggests that both a frontal and a parietal attention / disattention system, with connections between the two, are more effective in the highly hypnotizable individual. It has been demonstrated that hypnotizability may be a cognitive trait involving sustained and focused attentional abilities (Crawford et al., 1993; Lyons & Crawford, 1997; Tellegen & Atkinson, 1973). It has also been demonstrated that highly hypnotizable individuals exhibit more effective disattention or inhibitory abilities (e.g., Atkinson & Crawford, 1992; Crawford et al., 1993; E. R. Hilgard, 1965; Margolis et al., 1983), particularly when inhibiting the perception of pain (e.g., Crawford, Knebel, Kaplan, et al., 1998; E. R. Hilgard & J. R. Hilgard, 1994; Spiegel et al., 1989; Zachariae & Bjerring, 1994). It has been proposed that differences in brain dynamics (Crawford, 1994a, 1994b; Crawford et al., 1993; Crawford & Gruzelier, 1992; Crawford, Horton, Harrington, et al., 1998; Gruzelier & Warren, 1993) contribute to the highly hypnotizable individuals' better sustained attention and disattentional abilities (Atkinson & Crawford, 1992; Crawford et al., 1993). The more effective abilities of highly hypnotizable individuals are often observed in tasks involving sustained attention and requiring the disattention to distractions. Crawford et al. (1993) proposed that highly hypnotizable individuals have more flexible cognitive abilities that allows them to better allocate their resources for processing information, whether it requires attending to or disattending to stimuli (Crawford, 1994a, 1994b).

Our ongoing fMRI research (Crawford, Horton, Harrington, et al., 1998), from which participants were drawn for this morphological study, showed activation pattern differences between low and highly hypnotizable participants during hypnotic analgesia in the supplementary motor area, insula and anterior cingulate regions in the hemisphere contralateral to the experimental stimulation. There was also a reduction of activity in the somatosensory association cortex activity suggesting that hypnotic analgesia also impacted the sensory-discriminative system (see also Rainville et al., 1999). Crawford and colleagues (Crawford & Gruzelier, 1992; Crawford, Gur, et al., 1993; Crawford, Horton, Harrington, et al., 1998) suggested that the difference in neurophysiological activity seen in highly

hypnotizable individuals during hypnotic analgesia was indicative of the more effective inhibitory abilities of the highly hypnotizable participants. Since there was bilateral activation of the anterior frontal cortex during hypnotic analgesia, they further suggested that the highly hypnotizable individual's ability to inhibit pain was indicative of inhibitory effort that involved the anterior frontal cortex.

### Anterior Cingulate

Contrary to expectations, there were no significant volume differences in the anterior cingulate between low and highly hypnotizable individuals. However, the resolutions of the mid-sagittal images were not sufficient to accurately measure all of the anterior cingulate. As a result, the measurements used in this study were of only BA 24 and did not include BA 32. This resulted in volume measurements that were unsatisfactory for the comparative analysis of the anterior cingulate.

### Limitations of the Study

There are several limitations to this study. While our groups were both strongly right handed and drawn from a successfully functioning university population, our groups were not matched for IQ and thus we do not know if there was an influence from IQ. The overall number of participants was low. Power was increased by use of image measurements in lieu of participant measurements and by using a nested design ANOVA, but would have been increased by the addition of more participants. The MRI sequence resulted in T1 weighted images instead of T2 weighted images that resulted in less resolution and made identification of brain structures more difficult. Even though the interrater reliability was very high, a limitation to the study involved measurements being checked by an independent researcher trained by the principle investigator.

It is suggested that morphometric studies should be more sensitive to advances in image analysis by addressing four main components: 1) orientation normalization, 2) size normalization 3) well defined region delineation methods, and 4) metrics for defining shape

differences (personal communication, J. Hunter Downs, III, March 19, 1999). Thus far, CC studies have not necessarily included all of these components. The present study had well defined region delineation methods and employed orientation normalization of the sagittal plane by reorienting the horizontal axis to align the anterior commissure and posterior commissure to the same Y coordinates on the Scion Image (Scion Corporation) program. Future research also needs to reorient in two additional planes by aligning the anterior and posterior commissures in the axial and coronal planes, employ size normalization and address metrics for defining shape differences.

The present study used a geometric division of the CC based on Clarke et al.'s (1989) method of radial divisions. Since Clarke et al. did not separate the rostrum from the genu region, the rostrum was delineated and separated based on Witelson's (1989) method of straight-line division. Yet, another approach incorporated by Tan et al. (1991) may be more theoretically appropriate since it employed a more functionally oriented approach. In a study of commissurotomy patients, they electrically stimulated the CC intraoperatively at 1 cm intervals and recorded evoked potentials from different areas of the brain to determine topographical functional projections of the CC. They used the average length of 12 cm for the CC in man and subsequently divided the CC into approximate 1 cm sections. Tan et al. found that stimulation of the first four anterior CC segments resulted in evoked potentials not only in the anterior, middle, and posterior frontal lobe but also in the anterior and central temporal lobe. The first cm of CC seemed to be isolated with only the anterior portion of the frontal lobe equivalent to Witelson's (1989) division of region 1. Based on an average length of 12 cm, as established by Tan et al. (1991), the first 4 cm are approximately equivalent to Witelson's (1989) divisions of regions 1, 2, and the anterior portion of region 3 that comprise most of the anterior third of the CC. The first 6 - 7 cm would be approximately equivalent to the anterior half of the CC as divided by Witelson (1989). Replication of Tan et al. with additional patients would determine the generalizability of such divisions and contribute greatly to the development of more refined and functionally based division techniques.

### General Conclusions and Implications

The findings of this study support the hypothesized relationship of more effective neural processing in highly hypnotizable individuals (Crawford, Horton, & Lamas, 1998; Horton et al., 1998) in the orbitofrontal and parietal regions of the brain with increased brain structure volume in the rostrum and isthmus regions of the CC. The observed positive relationships between increased anterior CC volume and increased forebrain volume in highly hypnotizable participants but not low hypnotizable participants, support prior findings of more effective sustained and focused attentional abilities (Crawford et al., 1993) and inhibitory processes (e.g., E. R. Hilgard, 1965; Margolis et al., 1983). Since the morphological differences involve both the anterior and posterior attention and inhibition systems, these data especially suggest that they may be influential in facilitating highly hypnotizable individuals but not low hypnotizables to reduce or eliminate the perception of pain and distress.

This is the first morphological study to identify significant brain morphology differences between low and highly hypnotizable participants. The morphological differences of anterior and posterior regions of the CC in highly hypnotizable participants reflect the more effective anterior and posterior attentional systems in individuals who are highly hypnotizable, and lends support to the model proposed by Crawford (1994) and Crawford et al. (1993) and Crawford & Gruzelier (1992) suggesting differences in brain dynamics associated with hypnotizability.

Research involving morphological analyses of brain structures in participants diagnosed with ADHD, as compared to controls, provide an interesting comparison to the differential findings of brain structure morphology of low and highly hypnotizable participants. Highly hypnotizable participants demonstrated significantly larger rostrum, isthmus and right hemisphere splenium regions of the CC as compared to low hypnotizable participants. The same general areas of the CC were demonstrated to be significantly smaller in individuals diagnosed with ADHD (Baumgardner et al., 1996; Filipek et al., 1997; Giedd et al., 1994; Semrud-Clikeman et al., 1994). These combined data suggest a possible attention continuum in both the anterior and posterior attentional systems with significantly less volume of CC regions associated with ADHD on one end of the continuum to significantly more volume of CC regions associated with high hypnotizability on the other end of the continuum. Low hypnotizable individuals have significantly less volume of CC regions than highly

hypnotizable individuals and thus are more identifiable with some of the characteristics associated with ADHD individuals. It is noted once again only some common characteristics are involved and that they differ on other characteristics, therefore, these comparisons must be made with caution until further research is carried out. However, these data lend support to the idea of a possible genetic influence in attentional and inhibitory processes.

The morphological differences between low and high hypnotizables reported here raises the question whether there might also be a possible hereditary contribution to hypnotizability. Hypnotizability appears to be a highly stable cognitive / personality trait. There is high test-retest reliability for it over 25 years (Piccione, E. R. Hilgard, & Zimbardo, 1989). In general, it appears that hypnotizability is resistant to training (Barber, 1996, E. R. Hilgard & J. R. Hilgard, 1983).

Morgan (1973) compared hypnotizability in identical (monozygotic) twins, fraternal (dizygotic) twins, and non-twin sibling pairs. Monozygotic twins strongly resembled each other in hypnotizability (intra-class correlation of  $r' = .52$ ;  $N = 58$  pairs), whereas dizygotic twins did not ( $r' = .17$ ;  $N = 82$  pairs). Sibling pairs close together in age also did not show any significant relationship ( $r' = .19$ ;  $N = 132$  pairs). One caution to bear in mind is that one must always be concerned that identical twins may share a more common environment than fraternal twins may.

A study by Wallace and Persanyi (1989) examined the relationship between familial handedness and hypnotizability. They found that participants who had immediate relatives who were left handed scored lower on hypnotic susceptibility than participants who had immediate relatives who were right handed. When the immediate relatives of the participants were tested for hypnotic susceptibility, they found that the left handed relatives of participants scored lower on hypnotic susceptibility than did the right handed relatives of participants. They concluded that there might be a familial (genetic) influence on hypnotic susceptibility.

Recent Israeli research (Lichtenberg et al., under review) found in a group of 109 men and women that hypnotizability (measured by SHSS:C) correlates with the presence of the gene that codes for the activity of catechol-O-methyltransferase (COMT), an enzyme involved with dopaminergic and noradrenergic (but not serotonergic) metabolism. This polymorphism coding for high COMT activity was found to correlate with ADHD in a

previous study (Eisenberg et al., in press) and in their present study was associated with low hypnotizability. Furthermore, they found several subscales of the Differential Attentional Processes Inventory, that correlate with hypnotizability in their study as well as others (e.g., Crawford, Brown, & Moon, 1993; Lyons & Crawford, 1997). They also “showed a trend (non-conventional significance P values from 0.06 to 0.1) for the low COMT met allele to be associated with higher scores indicating extended ability in these individuals to divide attention.” They go on to suggest that “the role of the low enzyme activity COMT met allele in accounting for 10% of the variance in hypnotizability scores is likely mediated by this gene’s modulation of some aspects of central Executive Function, particularly dual attentional processes.” Working with these Israeli researchers, Crawford’s Neurocognition laboratory is presently involved in obtaining blood samples from those individuals who participated in the present morphological study to verify whether we can replicate these findings in highly hypnotizables individuals who can eliminate all perception of pain and low hypnotizables who cannot.

Black and Greenough (1991) emphasize the importance of socioenvironmental influences on genetic predispositions with their concept that genetic predispositions as, evidenced by specific alleles, expect to encounter certain types of environmental stimuli and are subsequently dependent on these stimuli for development. If these socioenvironmental influences are not encountered, neural development may take another route and develop in another direction. Thus, based on their concept of experience-expectant and experience-dependent development of neural plasticity, one may conclude that heritability factors in hypnotizability are plastic and may be influenced by an individual’s unique socioenvironmental situation (e.g., J. R. Hilgard, 1970, 1979; Nadon, Laurence, & Perry, 1989; Woody, Bowers, & Oakman, 1992), and be reflected in the different brain morphology of low and highly hypnotizable individuals and their ability to inhibit pain.

### Future Research

Some areas to be addressed in future research include expansion of areas involved in this study and investigation of other morphological relationships not addressed in this study. This

study measured the midsagittal image and an adjacent image from each hemisphere. In order to obtain a more accurate representation of the volume of each hemisphere, future research will use multiple images from the left and right hemispheres, measured more laterally into each hemisphere to better represent the hemispheric difference in volume of the brain structure of interest, and disregard the midsagittal image.

Future research is also planned to expand measurements of the anterior cingulate to include BA 24 and 32 instead of just BA 24, and to increase the number of images to be measured and extend image selection more laterally into each hemisphere. In the future it is also planned to divide the CC into smaller areas as an extension to the present study. Based on approaches used by Aboitz, et al. (1992) and Tan et al. (1991), the CC will be divided into smaller areas associated with a more functionally oriented approach that is more theoretically appropriate for morphometric analyses of CC involvement in cognitive processes.

Future research needs to address morphological differences of more specific areas of the forebrain with emphasis on BA 8, 9, 10, 11 12 & 13 to assess the relationship of these areas to the differential inhibitory abilities demonstrated by low and highly hypnotizable individuals. Future research also needs to address the possible relationship of the posterior cingulate to differential attentional abilities demonstrated by low and highly hypnotizable individuals. In addition, cerebellar morphology has been associated with pathology (Wassink et al., 1999) and should be addressed in future research with respect to relationship to differential attentional abilities demonstrated by low and highly hypnotizable individuals.

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Witelson, S. F. (1985). The brain connection: The corpus callosum is larger in left-handers. Science, *229*, 665-668.

Witelson, S. F. (1989). Hand and sex differences in the isthmus and genu of the human corpus callosum: A postmortem morphological study. Brain, *112*, 799-835.

Witelson, S. F., & Goldsmith, C. H. (1991). The relationship of hand preference to anatomy of the corpus callosum in men. Brain Research, *545*, 175-182.

Woody, E. Z, Bowers, K. S., Oakman, J. M. (1992). A conceptual analysis of hypnotic responsiveness: experience, individual differences, and context. In E. Fromm & M. R. Nash (Eds.), Contemporary hypnosis research (pp. 3-33). New York: Guilford Press.

Zachariae, R., & Bjerring, P. (1994). Laser-induced pain-related brain potentials and sensory pain ratings in high and low hypnotizable subjects during hypnotic suggestions of relaxation, dissociated imagery, focused analgesia, and placebo. International Journal of Clinical and Experimental Hypnosis, 42, 56-80.

Zaidel, E., Aboitiz, F., Clarke, J., Kaiser, D., & Matteson, R. (1995). Sex differences in interhemispheric relations for language. In F. L. Kitterle (Ed.), Hemispheric Communication: Mechanisms and Models (pp. 85-176), Hillsdale, New Jersey. Lawrence Erlbaum Associates, Inc.

## **CURRICULUM VITAE**

James E. Horton  
Phone: 423-538-5045  
365 Essex Drive  
Bluff City, Tennessee 37618

**EDUCATION:**           **Virginia Polytechnic Institute and State University,**  
Blacksburg, Virginia  
                                  Ph.D. degree in Psychology: May, 1999

**East Tennessee State University, Johnson City, Tennessee**  
                                  MA degree in Psychology: 1994  
                                  BS degree in Psychology: 1992

**Abilene Christian University, Abilene, Texas 1964 - 1967.**

### **PROFESSIONAL EXPERIENCE:**

Fall 1999                   **Clinch Valley College of the University of Virginia,**  
Wise, Virginia  
Appointed Assistant Professor of Psychology

Fall 1994 – Spring 1999: **Clinch Valley College of the University of Virginia,**  
Wise, Virginia  
Psychology Instructor

#### **Courses taught:**

Adolescent Psychology, Child Development, Cognitive Psychology, Developmental Theories, Experimental Psychology, Health Psychology, Human Sexuality, Human Neuropsychology, Introduction to Psychology, Personality Theories, Psychology of Learning, Research Methods, Sensation and Perception, Social Psychology and supervised Independent Studies.

Fall 1994 - Spring 1996: **East Tennessee State University,** Johnson City, Tennessee  
Adjunct Psychology Instructor

#### **Courses taught:**

Advanced General Psychology (six) and Psychology of Learning (one class).

Fall 1992 - Spring 1994: **East Tennessee State University,** Johnson City, Tennessee  
Teaching Assistant

#### **Courses taught:**

Advanced General Psychology Labs (six), Introductory Psychology (three classes) and Advanced General Psychology (one lecture class).

Aug 1993 - Nov 1993: **A-B-A-B Psychological Services & Counseling,**  
Bristol, Tennessee: Psychological Tester (Temporary)

## PUBLICATIONS

Asbury, E. T., Fritts, M. E., Horton, J. E., & Isaac, W. L. (1999). Progesterone facilitates the acquisition of avoidance learning and protects against subcortical neuronal death following prefrontal cortex ablation in the rat. Behavioural Brain Research, 97 (1) 99-106.

Crawford, H. J., Knebel, T., Vendemia, J. M. C., & Horton, J. E. (in press). La naturaleza de la analgesia hipnótica: bases y evidencias neurofisiológicas. Anales de psicología.

Crawford, H. J., Horton, J. E., Harrington, G. C., Vendemia, J. M. C., Plantec, M. B., Jung, S., Shamro, C., & Downs III, J. H. (1998) Hypnotic analgesia (disattending pain) impacts neuronal network activation: An fMRI study of noxious somatosensory TENS stimuli. Neuroimage, 7(4), S436.

Crawford, H. J., Horton, J. E., McClain-Furmanski, D., & Vendemia, J. (1998). Brain dynamic shifts during the elimination of perceived pain and distress: Neuroimaging studies of hypnotic analgesia. INABIS98, 0611.  
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Downs III, J. H., Crawford, H. J., Plantec, M. B., Horton, J. E., Vendemia, J. M. C., Harrington, G. C., Yung, S., & Shamro, C. (1998) Attention to painful somatosensory TENS stimuli: An fMRI study. Neuroimage, 7(4), S432.

Fritts, M. E., Asbury, E. T., Horton, J. E., & Isaac, W. L. (1998). Medial prefrontal cortex lesion deficits involving or sparing the prelimbic area in the rat. Physiology and Behavior, 64(3), 373-380.

## PUBLISHED ABSTRACTS

Crawford, H. J., Horton, J. E., Hirsch, T. B., Harrington, G. S., Plantec, M. B., Vendemia, J. M. C., Shamro, C., McClain-Furmanski, D., & Downs III, J. H. (1998) Attention and disattention (hypnotic analgesia) to painful somatosensory TENS stimuli differentially affects brain dynamics: A functional magnetic resonance imaging study. International Journal of Psychophysiology, 30(1-2), 77.

Crawford, H. J., Horton, J. E., & Lamas, J. (1998) Information processing speed is faster for highly hypnotizable than low hypnotizable persons: Evidence from behavioral reaction time and event-related potential studies. International Journal of Psychophysiology, 30(1-2), 84.

Horton, J. E., Lamas, J., & Crawford, H. J. (1998) Intending to ignore in waking and hypnosis: Influence of hypnotizability, sex, state and hand used on classic foreperiod reaction time effect. International Journal of Psychophysiology, 30(1-2), 238.

Horton, J. E., McClain-Furmanski, D., Mészáros, I., & Crawford, H. J. (1998) To inhibit pain is to actively shift conscious awareness: Somatosensory event-related potential evidence during hypnotic analgesia. International Journal of Psychophysiology, 30(1-2), 234-235.

## **BOOK REVIEWS**

Crawford, H. J., & Horton, J. E., (in press) Review of Brain Asymmetry by Richard J. Davidson and Kenneth Hugdahl (Eds.) in American Journal of Clinical Hypnosis (in press, 1998).

## **MANUSCRIPTS SUBMITTED FOR PUBLICATION**

Crawford, H. J., Knebel, T., Xie, M., Horton, J. E., & Pribram, K. H. (under review). Attentional Vs. Inhibitory (Hypnotic Analgesia) Processing of Noxious Stimuli: Somatosensory Event-Related Potential Amplitude and Latency Differences Between Low and Highly Hypnotizable Persons.

Horton, J. E., Bolling, Jr., J., Caudill, D., Hearld, W., & Moser, J. (1998) The phenomenon of road rage: The victim and the perpetrator. Under review.

## **MANUSCRIPTS IN PREPARATION**

Horton, J. E., Cook, D. A., & Isaac, W. L. (1999) Rat medial prefrontal cortex subfields: Associations of lesions with spatial maze and avoidance task performance.

Crawford, H. J., Horton, J. E., McClain-Furmanski, D., & Mészáros, I., (1999) Pain Inhibition due to an active shift of conscious awareness: Somatosensory event-related potential evidence during hypnotic analgesia.

Horton, J. E., Lamas, J., & Crawford, H. J., (1999) Influence of hypnotizability, sex, state and hand used on classic foreperiod reaction time effect while intentionally ignoring a warning signal during waking and hypnotic states.

Vendemia, J. M. C., Horton, J. E., & Crawford, H. J., (1999) Individual differences in physiological reactivity on an emotional Stroop interference task: Repressors and non-repressors.

## SCIENTIFIC MEETINGS: INVITED PRESENTATIONS

Crawford, H. J., Horton, J. E., Harrington, G. C., Hirsch, T. B., McClain-Furmanski, D., & Downs III, J. H. Hypnotic analgesia impacts cortical and subcortical pain networks: New evidence from somatosensory event-related potential and functional magnetic resonance imaging studies. Invited presentation in Neuroimaging of disattention and dissociation: Brain dynamic shifts symposium (chair: Helen J. Crawford), The 49<sup>th</sup> Annual Scientific Program of The Society for Clinical and Experimental Hypnosis, Chicago, Illinois, 1998.

Crawford, H. J., Horton, J. E., Hirsch, T. B., Harrington, G. S., Plantec, M. B., Vendemia, J. M. C., Shamro, C., McClain-Furmanski, D., & Downs III, J. H., (1998, September) Attention and disattention (hypnotic analgesia) to painful somatosensory TENS stimuli differentially affects brain dynamics: A functional magnetic resonance imaging study. Invited presentation in New perspectives in brain imaging of human pain control symposium (co-chairs: A. Chen and H. J. Crawford), The 9<sup>th</sup> World Congress of The International Organization of Psychophysiology (IOP), Taormina, Sicily, Italy, 1998.

Crawford, H. J., Horton, J. E., & Lamas, J., (1998, September) Information processing speed is faster for highly hypnotizable than low hypnotizable persons: Evidence from behavioral reaction time and event-related potential studies. Invited presentation in Attention and consciousness symposium (co-chairs: R. Näätänen and J. Kropotov), The 9<sup>th</sup> World Congress of The International Organization of Psychophysiology (IOP), Taormina, Sicily, Italy, 1998.

## SCIENTIFIC MEETING PRESENTATIONS: Peer Reviewed

McClain-Furmanski, D., Horton, J. E., & Crawford, H. J. (1999, April). Inhibition of pain: Effects on somatosensory event-related potentials during hypnotic analgesia in high but not low hypnotizable persons. Presented at Cognitive Neuroscience Society annual meeting, Washington, DC.

Horton, J. E., Lamas, J., & Crawford, H. J., (1998, September) Intending to ignore in waking and hypnosis: Influence of hypnotizability, sex, state and hand used on classic foreperiod reaction time effect. Presented at The 9<sup>th</sup> World Congress of The International Organization of Psychophysiology (IOP), Taormina, Sicily, Italy, 1998.

Horton, J. E., McClain-Furmanski, D., Mészáros, I., & Crawford, H. J., (1998, September) To inhibit pain is to actively shift conscious awareness: Somatosensory event-related potential evidence during hypnotic analgesia. Presented at The 9<sup>th</sup> World Congress of The International Organization of Psychophysiology (IOP), Taormina, Sicily, Italy, 1998.

Crawford, H. J., Horton, J. E., Harrington, G. C., Vendemia, J. M. C., Plantec, M. B., Jung, S., Shamro, C., & Downs III, J. H., (1998, June) Hypnotic analgesia (disattending pain) impacts neuronal network activation: An fMRI study of noxious somatosensory TENS stimuli. Presented at The 4<sup>th</sup> International Conference of Functional Mapping of The Human Brain, Montreal, Quebec, Canada, 1998.

Downs III, J. H., Crawford, H. J., Plantec, M. B., Horton, J. E., Vendemia, J. M. C., Harrington, G. C., Yung, S., & Shamro, C., (1998, June) Attention to painful somatosensory TENS stimuli: An fMRI study. Presented at The 4<sup>th</sup> International Conference of Functional Mapping of The Human Brain, Montreal, Quebec, Canada, 1998.

Horton, J. E., Lamas, J., Crawford, H. J., & Valle-Inclan, F., (1998, May) Intending to ignore: Influence of hypnotizability and state on classical foreperiod effect. Presented at The 10<sup>th</sup> Annual Convention of The American Psychological Society, Washington, DC, 1998.

Vendemia, J. M. C., Horton, J. E. & Crawford, H. J., (1998, May) Physiological reactivity of repressors and non-repressors on an emotional Stroop interference task. Presented at The 10<sup>th</sup> Annual Convention of The American Psychological Society, Washington, DC, 1998.

Bolling, Jr., J., Caudill, D., Church, D., Gent, J., Hearld, W., Moser, J. Erin, S. & Horton, J. E. (1998 March) The phenomenon of road rage: Have you ever been a victim or perpetrator? Presented at the 44<sup>th</sup> Annual Meeting of the Southeastern Psychological Association, Mobile, AL, 1998.

Horton, J. E., Cook, D. A., Williams, S. A., & Isaac, W. L. (1995, March) Rat prefrontal cortex subfields: Lesions and maze task performance. Presented at The 41st Annual Meeting: Southeastern Psychological Association, Savannah, GA, 1995.

Cook, D. A., Williams, S. A., Horton, J. E., & Isaac, W. L. (1995, March) Lesions of the rat prefrontal cortical subfields: Four-way avoidance performance. Presented at The 41st Annual Meeting: Southeastern Psychological Association, Savannah, GA, 1995.

Fritts, M. E., Horton, J. E., Asbury, E. R., & Isaac, W. L. (1994, March) Rats, occipital lesions and recovery: Sensory stimulation facilitates avoidance responses. Presented at The 40th Annual Meeting: Southeastern Psychological Association, New Orleans, LA, 1994.

Horton, J. E., Asbury, E. T., Fritts, M. E., Amos, N. G., Cook, D. A., & Isaac, W. L. (1993, November) Effects of medial frontal cortex lesions in rats involving or sparing the prelimbic area on the acquisition of an 8-arm maze task. Presented at The 23rd Annual Meeting: Society for Neuroscience, Washington, DC, 1993.

## **GRANTS**

Virginia Polytechnic Institute & State University Graduate Student Assembly Organization Travel Grant, 1998

Society of Clinical and Experimental Hypnosis Scholarship Grant, 1998

## **COLLEGE SERVICE**

### **Committee Service**

(Aug 1990 - Aug 1994): Member of the Center of Adult Programs and Services Action Committee at ETSU and served on the search committee for the director of the Center of Adult Programs and Services.

(1997 – Present): Member of the academic appeals committee, Clinch Valley College.

### **Peer Mentoring**

(Aug 1990 - Aug 1994): Peer mentor at the Center for Adult Programs and Services at ETSU and was involved in Adult orientation by speaking to reentry adults and assisting in orientation check in and campus tours.

### **Science Fair**

(Fall 1992 - Spring 1994): Assisted children participating in the science fair at ETSU by advising them regarding their experimental project planning, designs and methodology.

## **COMMUNITY SERVICE**

### **Scouting**

(1994 - Present): Active in scouting programs as a past Scoutmaster and currently in a church related scouting program as a Commander in the Royal Rangers.

### **Counseling**

(1990 - Present): Volunteer youth counselor working with teenagers in my local church and worked with teenage boys from the Jacobs Creek Job Corp. I led group discussions, taught Bible study classes and counseled some of the boys on an individual basis.

### **Church**

(1984 - Present): Teach occasional Sunday School Classes and lead discussions in Adult Bible study groups. I also serve as an usher and a member of the Board of Directors.

## **WORKSHOPS ATTENDED**

fMRI workshop on Functional MRI. (March, 1997), Boston, MA

NSF/NIMH/NIH APS Workshop on Writing Research Grant Proposals. (May 1998).  
American Psychological Society 10<sup>th</sup> Annual Convention, Washington, DC.

New Directions in Pain Research (November, 1997), NIH, Bethesda, MD.

Neuroscan Workshop on Multimodal Neuroimaging. (April, 1998), NIH, Bethesda, MD.

Hypnotherapy for Pain and the Treatment of Burns. (November, 1998), The Society for  
Clinical and Experimental Hypnosis 49<sup>th</sup> Annual Workshops and Scientific Program,  
Chicago, Illinois.

Dissociative Disorders. (November, 1998), The Society for Clinical and Experimental  
Hypnosis 49<sup>th</sup> Annual Workshops and Scientific Program, Chicago, Illinois.

## **MEMBERSHIPS**

American Psychological Society, 1998 - Present

Cognitive Neuroscience Society, 1997 - Present

International Organization of Psychophysiology, 1998 - Present

Psi Chi, 1993 - Present

Society for Clinical and Experimental Hypnosis, 1998 - Present

Southeastern Psychological Association, 1993 - Present

Society for Psychophysiological Research, 1997 - Present