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# Magnetic Resonance Imaging Volumetric Analysis of the Putamen in Children With ADHD

## Combined Type Versus Control

Tasha McMahon Wellington
Margaret Semrud-Clikeman
Amanda Louise Gregory
*University of Texas, Austin*
Jennifer Mary Murphy
*University of California, San Francisco*
Jack Lynn Lancaster
*University of Texas, San Antonio*

**Objective:** Volumetric differences in the putamen of boys with ADHD combined subtype with psychopathic traits and controls are investigated. **Method:** The putamen in 24 archival magnetic resonance imaging scans of 12 boys in residential treatment with symptoms of ADHD and psychopathic traits and 12 community control boys are analyzed using Display software. **Results:** There are no differences found in the total, left, and right putamen volumes across the ADHD or control group. A significant reversal of asymmetry across groups is found; children with ADHD more frequently have a smaller left putamen than right. In contrast, the control group more frequently has a smaller right than left putamen. **Conclusion:** A reversal of symmetry in the putamen (as found in the caudate) may relate to ADHD symptomology as well as to psychopathic traits. *(J. of Att. Dis. 2006; 10(2) 171-180)*

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ADHD is a childhood onset psychiatric disorder with a complex and heterogeneous etiology comprising genetic, neurobiological, prenatal, and environmental factors (Mercugliano, 1999; Wagner, 2000). ADHD is defined by age-inappropriate excessive observable behaviors such as short attention span, hyperactivity, and distractibility (Mercugliano, 1999). The externalizing behaviors in ADHD account for 50% of referrals to treatment (Cantwell, 1996; Casey et al., 1997; Schachar, Tannock, Marriott, & Logan, 1995). It is considered one of the most prevalent psychiatric problems occurring in children with a prevalence of 5% to 10% of school-age children (Casey et al., 1997) and has even been estimated as high as 18% (Baumgaertel, Wolraich, & Dietrich, 1995). Fifty percent to 78% of children with ADHD continue to have difficulty in adolescence and adulthood with concentration, impulsivity, irritability, and anxiety, all of which contribute to poor social relations and work impairments (Casey et al., 1997; Hechtman, 1999). Approximately 10% to 15% of children with ADHD have been found to display psychiatric and/or antisocial problems in adulthood (Hechtman, 1999). The course of ADHD is often chronic, disrupting the child's development and functioning, contributing to future psychiatric and social difficulties (Cantwell, 1996).

Understanding the underlying neurological underpinnings of ADHD is important for the design of effective psychological and pharmacological interventions. The neurobiology of ADHD can be explored with three different approaches: neuropsychological, neurochemical, and neuroanatomical (Riccio, Hynd, Cohen, & Gonzalez, 1993). Evidence from all three disciplines has found structural and functional abnormalities in the basal ganglia of children with ADHD (Castellanos, 1997; Filipek et al., 1997; Mercugliano, 1999).

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Address correspondence to Tasha McMahon Wellington, Department of Psychology, University of Texas at Austin, Austin TX, 78712; e-mail: mcmahont@mail.utexas.edu.

## Neurobiology of ADHD

Teeter and Semrud-Clikeman (1995) describe at least 11 different neuroanatomical theories of ADHD. These theories can be categorized into two domains. The "bottom-up" theories propose disturbances in subcortical regions, such as the thalamus, and hypothalamus and reticular activating systems are responsible for ADHD symptomology. The "top-down" theories attribute the dysfunction to frontal and prefrontal and sagittal cortices (Teeter & Semrud-Clikeman, 1995). Neuroimaging studies of children with ADHD have investigated and found evidence of abnormalities in the frontal cortex, basal ganglia, corpus callosum, and cerebellum (Castellanos et al., 2001; Castellanos et al., 1996; Hendren, De Backer, & Pandina, 2000; Semrud-Clikeman et al., 1994). Preliminary evidence has not found differences in the thalamus in children with ADHD (Castellanos et al., 1996; Filipek et al., 1997).

## The Role of the Basal Ganglia in ADHD

The basal ganglia is a collection of large subcortical structures that can be divided into two sets of core structures: (a) the striatum consisting of the caudate, putamen, and ventral striatum and (b) the pallidum or globus pallidus consisting of the external segment, internal segment, and ventral pallidum. The striatum receives input from the entire cerebral cortex, thalamus, substantia nigra, and amygdala and sends projections to the pallidum and substantia nigra. The pallidum sends input to the thalamic nuclei and additional subcortical nuclei, where information will be sent back to the frontal or prefrontal cortex (Parent, 1996). The organization of the striatum is important in the execution of motor planning, sequencing, and coordination, as well as feedback and learning after motor execution. Teicher, Anderson, Glod, Maas, and Renshaw (2000) suggest that the striatum serves as a "crossroads," combining sensorimotor information with emotional processing from the amygdala and dopamine-mediated reinforcement.

The primary neurotransmitter involved in modulation of the basal ganglia is dopamine, and disruption of this system has been found in ADHD. Initial studies found higher levels of the dopamine metabolite, and homovanillic acid in cerebral spinal fluid were positively correlated with the amount of hyperactivity in boys (Castellanos et al., 1996). A recent genetic study found that alleles of the gene encoding dopamine beta hydroxylase, an enzyme that breaks down dopamine, may be related to the expression of ADHD (Navia et al., 2000). Further support for dopamine dysfunction in ADHD comes from a functional magnetic resonance imaging (MRI) study that found children with ADHD had reduced activity in the frontal-striatal regions and impaired performance on a response inhibition tasks (Vaidya et al., 1998). Additionally, methylphenidate, which acts on the dopamine transporter (DAT), increased both frontal-striatal activity and performance on response inhibition tasks. A study using Single Photon Emission Computed Tomography found that adults with ADHD had increased levels of striatal DAT compared to normal controls, which may lead to decreased availability of striatal dopamine in ADHD (Krause, Dresel, Krause, Kung, & Tatsch, 2000).

Research on the role of the basal ganglia in ADHD has primarily focused on the caudate. The caudate has been implicated in a "complex loop," receiving information from the association cortices and indirectly sending it via the thalamus to the prefrontal cortex (Saint-Cyr, Taylor, & Nicholson, 1995). Studies have found neuroanatomical differences in the caudate of children with ADHD with mixed results (Casey et al., 1997; Castellanos et al., 2001; Castellanos et al., 1996; Hynd et al., 1993; Mataro, 1997; Semrud-Clikeman et al., 2000). Castellanos et al. (1996) found that boys with ADHD had a smaller right caudate; recently, this finding was not replicated in ADHD girls (Castellanos et al., 2001). In boys with ADHD, smaller right caudate volumes were found to significantly correlate with poor accuracy on sensory selection (forced-choice discrimination) tasks, and left and right caudate volumes were negatively correlated with mean reaction times (Casey et al., 1997).

Conflicting results found ADHD adolescents had larger right caudate than normal adolescents, and the right caudate volume was associated with poorer performance on attention tasks and higher ratings of hyperactivity and impulsivity (Mataro, 1997). Studies by Hynd et al. (1993) and Filipek et al., (1997) found that children with ADHD had smaller left caudate volumes. More recently, Semrud-Clikeman et al. (2000) reported that boys with Attention Deficit Disorder with Hyperactivity were found to have a decreased volume of the left head of the caudate. These children were also more likely to show a reversed caudate asymmetry when compared to healthy controls, with the left being smaller than right. Moreover, a significant relationship between the reduction in left caudate volume and performance on behavioral inhibition tasks was found. In addition, children displaying reversed caudate asymmetry ($L < R$) were more likely to perform poorly on tasks of behavioral inhibition and attention regardless of group membership (Semrud-Clikeman et al., 2000).

Casey et al. (1997) also previously found that reversed caudate asymmetry was related to deficits in response execution tasks in ADHD. This evidence suggests that asymmetry of the caudate regardless of volume has important implications in attention and behavioral control. Finally, functional imaging studies have found decreases in blood flow to the caudate in ADHD (Castellanos et al., 1996; Peterson, 1995).

## The Role of the Putamen in ADHD

The putamen is hypothesized to be part of the "motor loop" because it receives information from the sensorimotor cortex and then sends it indirectly back to the premotor regions of the frontal cortex. Based on the putamen's anatomical connections and function, a role for the putamen in ADHD is possible although currently unclear because of equivocal evidence (Saint-Cyr et al., 1995). There are relatively few studies investigating the neuroanatomical role of the putamen in ADHD. Castellanos et al. (2001) and Castellanos et al. (1996) have not found volumetric differences in the putamen between children with ADHD and healthy controls. In addition, they found that the volume of the putamen did not correlate with performance on response inhibition tasks. However, two studies suggest that the putamen may actually be important in the expression of ADHD symptomology. Peterson et al. (2000) found that the ADHD diagnosis was significantly associated with titer of two antistreptococcal antibodies. In addition, they found that higher antibodies titers were associated with larger volumes in the left putamen and right globus pallidus in children with ADHD (Peterson et al., 2000). Although this study found structural evidence for the role of the putamen in ADHD, the second study demonstrates functional differences in the putamen of children with ADHD.

Recent advances in functional MRI technology have provided new methods to investigate blood flow to various regions of the brain. Functional MRI relaxometry allows researchers to investigate the resting or steady-state conditions and medication-related changes (Teicher et al., 2000). Teicher et al. (2000) were able to indirectly assess blood volume to the striatum (caudate and putamen). They found that blood flow to both sides of the putamen was decreased in ADHD children compared to normal children. In addition, they found that blood flow to the left was more decreased than blood flow to the right side. They found no differences in blood flow to the thalamus and caudate, although there was a nonsignificant trend in the right caudate. Methylphenidate administration significantly altered the blood flow to the right and left putamen, and changes were correlated to the child's unmedicated state. There were no significant differences in blood flow to the caudate off or on medication. Teicher et al. (2000) found strong associations between measures of activity and inattention with T2-RT measures in the putamen. They propose that ADHD symptoms are closely related to functional abnormalities in the putamen, which is closely involved in the control of motor behavior. These hypotheses lay the foundation for our study of the neuroanatomy of the putamen in children with ADHD.

## Objective of Present Study

Structural and functional imaging studies have provided evidence for the role of basal ganglia abnormalities in ADHD. Although previous studies by Castellanos et al. (2001) and Castellanos et al. (1996) have not found differences in the putamen, more recent work has suggested a possible role for the putamen in ADHD (Teicher et al., 2000). The purpose of this study was to evaluate the volume and asymmetry of the putamen. The asymmetry measure is important given that previous research has found differences in asymmetry measures in the caudate and suggested that the reversal in asymmetry may lead to abnormalities in the underlying neurotransmitter systems (Hynd et al., 1993) and may affect the ability to regulate behavior.

## Method

### Participants

This study used participants from a previous study interested in neuropsychological functioning that used both participants with ADHD: combined type (CT) and ADHD predominately inattentive type. The original sample consisted of 44 male participants, with 25 recruited from a residential treatment center and having comorbid ADHD and psychopathic traits and 19 healthy community controls. From the possible 25 male participants, 12 were selected who were diagnosed with ADHD combined subtype. The remaining 12 had been diagnosed with ADHD predominately inattentive subtype, and 1 participant was excluded because of incomplete MRI and neuropsychological data. From a possible 19 normal healthy control participants, 12 were selected because of being free from ADHD symptomology, whereas the remaining 6 demonstrated significant symptoms of ADHD, and 1 community participant was excluded from the study because of an abnormality on MRI.

The 12 males with comorbid ADHD CT and psychopathic traits were recruited from an adolescent residential psychiatric facility in the Southwest (Gregory, 2001;

Murphy, 2001). The diagnosis was obtained from the treatment center, and the number of ADHD symptoms was available for these participants, and all 12 participants met criteria for ADHD CT based on *Diagnostic and Statistical Manual of Mental Disorder* (4th ed.; American Psychiatric Association, 1994) criteria. A mean prorated Full Scale IQ of 94.5 ($SD = 9.2$) was found for the ADHD group. This sample is heterogeneous diagnostically; a significant number of participants were experiencing mild levels of depressive symptoms, had learning delays, and all had psychopathic traits. Children with anxiety disorders or mania or psychoticism were not accepted for the original study, and the adolescents were supervised by an on-site psychiatrist for medication monitoring while participating in the study.

The ADHD CT children had comorbid psychopathic traits assessed by the Psychopathy Checklist–Youth Version (PCL-YV; Forth, Kosson, & Hare, 1997), with a mean of 28.5 ($SD = 5.2$) and a range of 19 to 36. Only 3 participants met criteria for psychopathy with a score of 30 or greater (the cutoff for psychopathy is 30). Thirty-six percent of the sample demonstrated mild to moderate levels of psychopathic characteristics (moderate psychopathy risk), with PCL-YV scores ranging from 19 to 24, whereas 63% of the sample showed high levels of psychopathic characteristics (high psychopathy risk), scoring 28 to 36 on the PCL-YV.

The control group consisted of 12 male participants ages 13 to 17 ($M = 14.7$, $SD = 1.5$) with no ADHD symptomology, as determined by the Structured Interview for Diagnostic Assessment for Children (SIDAC). This 30-min interview was conducted with community participants by master's-level doctoral students in clinical psychology to screen for comorbid disorders. The number of symptoms of ADHD was available for all the healthy normal controls. These 12 participants did not meet criteria for a diagnosis of ADHD, depression, mania, anxiety, or psychosis based on the SIDAC. This control sample had a mean Full Scale IQ of 118.7 ($SD = 19.5$). In addition, these participants were free from elevated psychopathy traits, based on the PCL-YV ($M = 0.91$, $SD = 1.3$), with a range of 0 to 4, and more than 50% of the sample obtained a score of 0 (see Table 1).

In the sample, there were no significant differences in parental years of education between ADHD participants ($M = 14.4$, $SD = 2.3$) and the control group ($M = 15.7$, $SD = 2.3$) or for age, $F(1, 22) = .071$, $p = .792$, or ethnicity, with all participants being primarily Caucasian. There were significant differences in the prorated Full Scale IQ between the ADHD participants and the control group, $F(1, 22) = 12.1$, $p = .002$.

**Table 1**
**Participant Characteristics**

| | Control ($n$ = 12) | | ADHD ($n$ = 12) | |
|---|---|---|---|---|
| Variable | *M* | *SD* | *M* | *SD* |
| Age | 15.7 | 2.3 | 14.4 | 2.3 |
| Full Scale IQ | 118.7 | 19.5 | 94.5 | 9.2* |
| Psychopathic traits | 0.91 | 1.3 | 28.5 | 5.2* |
| Socioeconomic status | 15.73 | 2.5 | 14.4 | 2.5 |

*$p < .02$.

The study participants met the following criteria to participate: (a) no history of inhalant abuse; (b) no history of significant head injury (loss of consciousness greater than 5 min); (c) no current sinus problems or history of respiratory disease; (d) no history of psychotic symptoms; (e) IQ estimates, based on prorating Wechsler Intelligence Scale for Children (3rd ed.; Wechsler, 1991) Block Design and Vocabulary subtest scores, of 75 or higher; (f) no gross abnormalities on MRI (e.g. tumors); (g) no claustrophobia or metallic implants, to ensure safety during the MRI; and (h) English as a first language (Gregory, 2001).

## Image Acquisition

All MRI scans were acquired with a 1.5 Tesla General Electric Signa scanner (GE Medical Systems, Milwaukee). Low resolution axial spoiled gradient (SPGR) sagittal localizer images were obtained first, followed by 4 mm contiguous axial spin echoes (repetition time [TR] = 2,000, echo times [TEs] = 30 and 80, number of excitations [NEX] = 1, field of view [FOV] = 28) for calculating T2 relaxation times and image contrast. Contiguous 1.2mm-thick SPGR 3D volume sagittal slices were acquired last. Sagittal acquisition permitted thin slices that covered the whole brain in one pass. Technical parameters were TR = 24, TE = 5, flip angle = 40 degrees, matrix + 192 x 256, NEX = 2, FOV = 30 cm, number of slices = 128, and frequency encoding direction = superior/inferior. GE software minimizes distortion when reformatting images to the coronal plane because voxels are nearly isotropic (1.17 x 1.17 x 1.2 mm). A certified neurologist evaluated all 24 MRIs and found no gross abnormalities. Raw images were stored on DAT tapes.

## Image Analysis

Raw images were processed on Silicon Graphics computer workstations. The brains were oriented along the posterior and anterior commissures and reformatted into a coronal 1.0 mm positionally normalized scan to account for differences in the head position at the time of the image acquisition. This reformatting also spatially normalized to a standard brain size to allow for comparison of brain region volumes while controlling for developmental size differences. These images were converted into MINC (Medical Image NetCDF) files and stored on compact disc.

Volumetric analysis of the images in MINC format was done using a PC version of Display Software developed at Montreal Neurological Institute. Anatomic segmentation was performed in three dimensions: coronal, sagittal, and horizontal planes. Each normalized image intensity contour algorithms were kept constant across all images to control for potential differences caused by voxel intensity. Brain regions were to be highlighted, and the volume of the highlighted region calculated. Highlighting was done and double checked in all three dimensions, using a paint brush size of 1 voxel (1 mm). Volumetric analysis was done blind to the child's diagnosis.

Guidelines for anatomical boundaries of putamen were taken from Mai, Assheuer, and Paxinos (1997) and DeArmond, Fusco, and Dewey (1989). The putamen is the largest and most lateral region of the corpus striatum. It is bounded laterally by the external capsule and medially by lateral medullary lamina of the globus pallidus and more medially by the external globus pallidus. Anterior commissure was used as a landmark to help determine the medial and ventral putamen boundaries. Care was taken to exclude the accumbens nuclei as it lies between the caudate and putamen in the coronal sections (see Figure 1).

## Statistical Analysis

All scans were measured blind to participants' condition by one rater, and intrarater reliability on 16% (5 out 24 scans) of the images was 0.89, which was within reliability measures found on other studies (Castellanos et al., 2001; Castellanos et al., 1996). Group assignment was unblinded after volumetric measurements were completed. Analysis of the putamen volumes was completed using a split plot design in Statistical Package for the Social Sciences with ADHD/psychopathy traits versus control as the between-subject measure and asymmetry (right minus left) as a within-subject measure. A univariate analysis on the asymmetry data was run to verify the split plot results.

The asymmetry measure was analyzed in two forms: raw score (right putamen minus left putamen) and a scale using a symmetry coefficient (R-L)/.05(R+L) (Castellanos et al., 1996; Semrud-Clikeman et al., 2000). Analysis was run with and without controlling for Full Scale IQ (FSIQ). It was not possible to run a regression or to control for psychopathic traits on these data given the restricted range of psychopathic traits within each group.

## Procedure

MRI scans were acquired from two previous studies on psychopathy and brain abnormalities (Gregory, 2001; Murphy, 2001). Twenty-four archival images were selected, 12 with ADHD CT and 12 control children (ADHD free). Blind measurements of the putamen volume were made using Display software and then sorted into ADHD CT or control group membership. The data collected were in cubic centimeters. These data were analyzed with a split plot design.

# Results

Results for each of the three hypotheses are illustrated in Figures 2 and 3, respectively. Results from the spilt plot analysis found no significant volumetric differences between groups for total, right, and left putamen measures, $F(1, 22) = .120$, $p = .732$.

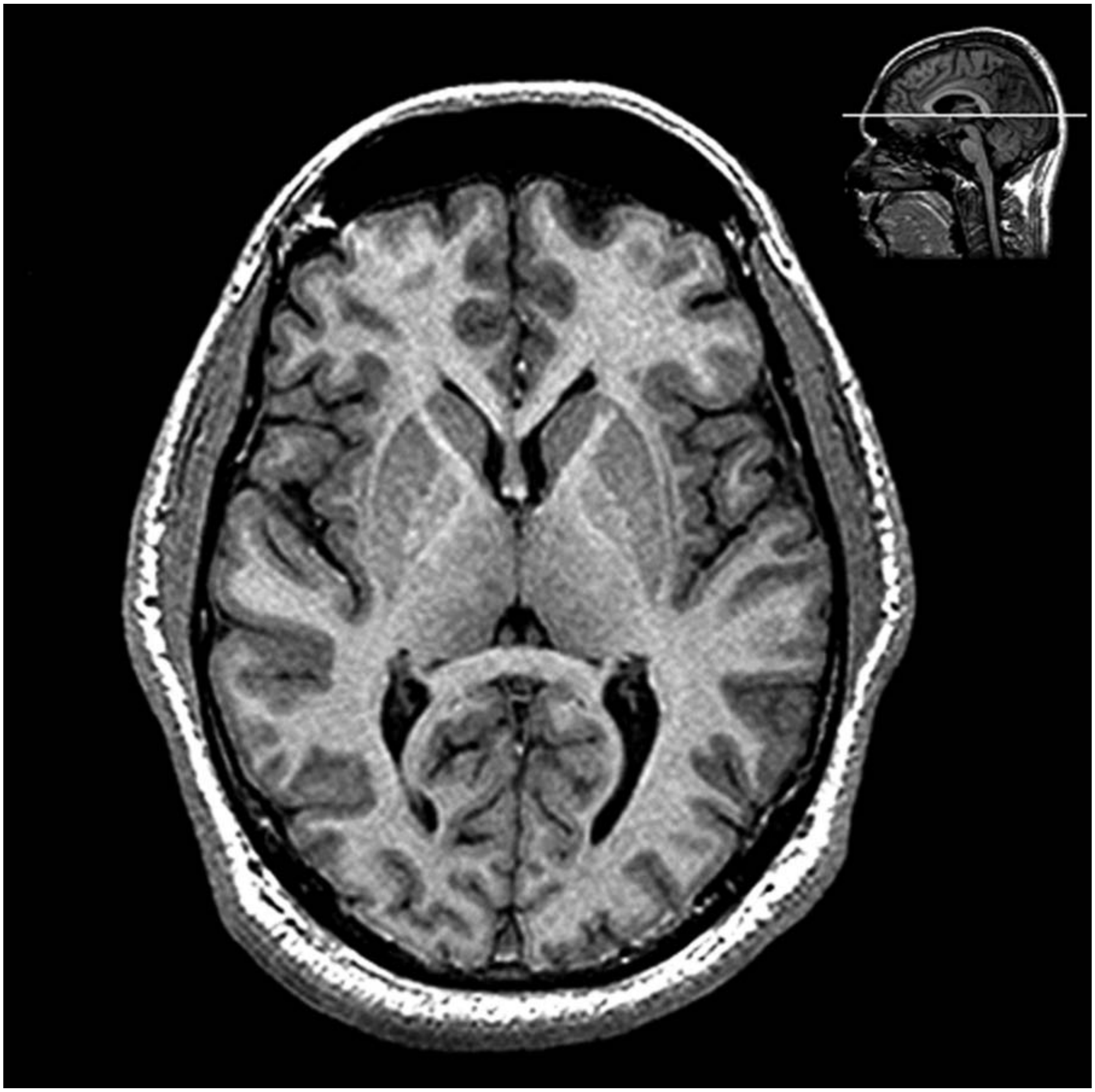
The split plot analysis found a significant interaction between the side (right versus left) of the putamen and group membership (ADHD CT versus control). This finding was confirmed with a univariate ANOVA. There was a significant difference in right and left asymmetry of the putamen, $F(1, 22) = 4.925$, $p = .036$, such that ADHD CT children had a larger right than left putamen ($M$ = 0.0995, $SD$ = 0.181), whereas controls had a smaller right than left putamen ($M$ = –0.073, $SD$ = 0.22). After controlling for FSIQ, this result remained significant, $F(1, 22) = 5.925$, $p = .025$. In addition, when the univariate ANOVA was run using the asymmetry coefficients as described by Semrud-Clikeman et al. (2000) and Castellanos et al. (1996), the difference in asymmetry between ADHD CT children ($M$ = 3.10, $SD$ = 3.49) and normal control children ($M$ = –1.37, $SD$ = 4.95) again remained significant, $F(1, 22) = 6.297$, $p = .021$. These results suggest that children with ADHD CT had a reversal of asymmetry in the putamen when compared to control children.

Observed power was .569 for asymmetry, and the effect size was .40 without controlling for FSIQ.

# Discussion

The present study examined MRI scans of the putamen, a component of the basal ganglia associated with motor control, in children with ADHD CT and nor-

**Figure 1**
**Horizontal Cross-Section of the Basal Ganglia**



Note: The putamen is bounded laterally by the extreme capsule and medially by the external capsule. It lies lateral to the globus pallidus. Figure reproduced with permission from the Digital Anatomist Project, University of Washington.

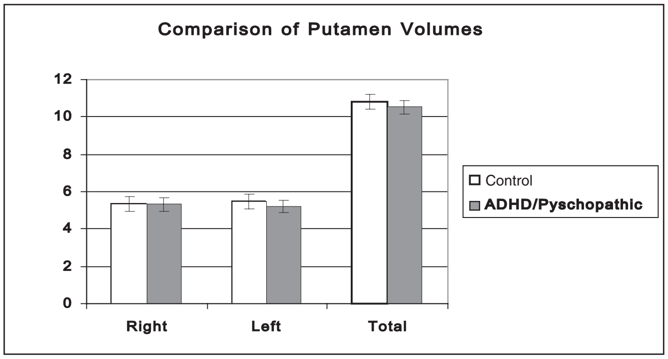
mal controls. The volume of the left, right, and total putamen were calculated. These measures and the asymmetry of the putamen were compared in these two groups. The hypotheses of the present study were that there would be differences in total and left volume of the putamen, such that these measures would be smaller in the ADHD CT and psychopathic traits group. It was hypothesized that asymmetry of the putamen would be reversed in children with ADHD CT and comorbid psychopathic traits compared to controls.

The present study found no differences in the total, left, or right volumes of the putamen between groups. However, there was support for the hypothesis for the reversal of symmetry in the ADHD group when compared to control, such that there was side versus group interaction. Children in the ADHD group more often had a larger right putamen than left, whereas control children had larger left putamen than right.

## Implications

The lack of any significant differences in total, left, and right volume of the putamen between ADHD and control is supported by previous studies (Casey et al., 1997; Castellanos et al., 2001; Castellanos et al., 1996). No previous research has reported any differences in the symme-

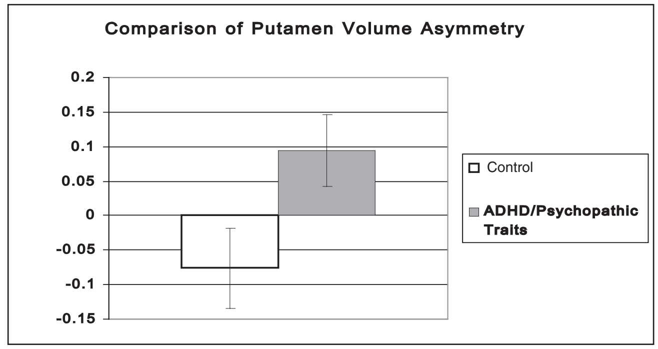
**Figure 2**
**The Mean Volume and Standard Deviations for Total, Right, and Left Putamen**




Volume in cubic cm

Note: No significant difference was found between the control and ADHD groups ($p > .05$).

**Figure 3**
**The Mean Right Minus Left Putamen Differences Scores and Standard Deviations**




Right - Left Difference Score

Note: A significant difference was found between the control and ADHD groups ($p = .036$).

try of the putamen. However, the finding of reversal of symmetry is indirectly supported by the finding of decreased blood flow to the putamen, particularly to the left side (Teicher et al., 2000). In addition, they did not find a significant decrease in blood flow to the caudate, which has previously been implicated as the primary site of dysfunction in ADHD. Teicher et al. (2000) found that measures of hyperactivity and inattention could be accounted for by deficits in blood flow to the putamen alone, and the deficits in blood flow and behavior were both attenuated by methylphenidate. Current studies found that putamen lesions from strokes and traumatic brain injury are related to the development of secondary attention deficit disorder (Gerring et al., 2000; Max et al., 2002). Therefore, it is possible that the reversal of symmetry found in the putamen might contribute to motor symptoms seen in ADHD CT. These findings, along with the function of the putamen, suggest the possibility that putamen abnormalities are related to symptoms of impulsivity and hyperactivity being expressed in this population of children. Together, these results suggest that structural and/or functional abnormalities of the putamen may play a role in hyperactivity symptoms seen in ADHD, which is consistent with the putamen's direct involvement in regulation of motor activity. It is possible that the reversal in asymmetry is contributing to a regulation of motor output in the ADHD CT versus normal children.

This study examined ADHD children who also had comorbid psychopathy traits, with three meeting the cutoff for psychopathy; therefore, these findings may relate to comorbidity of these psychiatric disorders. Previous studies of adolescents with ADHD and conduct disorder (CD) symptoms have found that these adolescents have more deficits in monitoring their ongoing behavior than ADHD or CD alone (Clark, Prior, & Kinsella, 2000). Therefore, it is likely that children with ADHD and comorbid antisocial behaviors exhibit more severe underlying neurological deficits and as a result, have more brain regions affected than either disorder expressed alone. This finding is supported by a recent study by Pineda et al. (2002) that found no caudate differences between children without ADHD and children with ADHD: inattentive type or ADHD CT. They suggest that previous findings related to reversal of caudate asymmetry in children with ADHD may be the result of comorbidity of learning disorders in the samples, although several of the research studies on the caudate ruled out learning disorders (Filipek et al., 1997; Hynd et al., 1993). Given that ADHD has a high rate of comorbidity with other neuropsychological disorders, the impact of comorbidity on brain structures requires further research.

The present study, along with previous findings (Gerring et al., 2000; Max et al, 2002; Peterson et al., 2000; Teicher et al., 2000), suggests that the role of the putamen abnormalities should continue to be investigated to fully understand the mechanisms involved in the expression of hyperactivity and inattention. Attention to dysfunction in the putamen should be considered when working toward pharmacological and psychological interventions in children with ADHD with comorbid disorders. Given the plethora of connections between the putamen and the caudate, asymmetry of the putamen may in concert with caudate differences contribute to the expression of symptoms of hyperactivity and impulsivity as demonstrated by the children in this sample.

## Limitations

The primary limitation of this study is the comorbidity of psychopathy traits, which may contribute to the reversed asymmetry of the putamen. Given that there was such a restricted range of psychopathic traits in both the control and ADHD group, it was not possible to run a regression to try to tease out the impact of the psychopathic traits in this sample. A brief review of the neurophysiological and neuroanatomical literature on antisocial and violent behavior did not find a current evidence of putamen dysfunctions in psychopathy traits. The brain regions that are currently implicated in psychopathy, such as lack of empathy and antisocial behavior, are frontal/prefrontal cortex, thalamus, amygdale, hippocampus, and other limbic structures (Gregory, 2001; Laakso et al., 2001; Murphy, 2001; Raine, Lencz, Bihrle, LaCasse, & Colletti, 2001).

Given the comorbidity issue and the severity of symptoms requiring residential treatment, this subset of children may have different underlying neurological pathology related to the comorbidity of ADHD and psychopathic traits; to disentangle this confound, two additional groups should be analyzed: children with ADHD CT only and a group with psychopathic traits only. This procedure would allow for a complete analysis of the role of putamen dysfunction in ADHD versus psychopath traits.

As previously stated, this sample is heterogeneous diagnostically, and in this study, there may be some individuals who are scoring high on the PCL-YV because of external factors such as abuse that may not develop into adult psychopaths if adequate early intervention is enacted. To investigate this possibility, we evaluated the relationship between abuse and PCL scores. In the current sample, abuse (physical or sexual) was correlated with PCL scores ($r = .40$). Although these factors make generalization issues more difficult, the sample is certainly an ecologically valid one from the perspective of addressing the needs of troubled adolescents currently seeking treatment.

## Conclusion

Future studies should specifically examine the role of putamen symmetry in relation to ADHD subtypes, symptom severity, and comorbidity. Behavioral measures of hyperactivity, inattention, and a number of ADHD symptoms need to be included to investigate the correlation between these symptoms and the putamen. The particular finding of asymmetry of the putamen specific to ADHD CT comorbid with psychopathic traits suggests that the underlying neurological deficits in these children may be different from a child with a sole diagnosis of ADHD. This study and recent studies also suggest that there may be a role for the putamen in expression of ADHD-related symptoms, such as inattentive, impulsivity, and hyperactivity, which requires further investigation. Brain abnormalities have important implications for both pharmacological and psychological treatment (Semrud-Clikeman et al., 2000; Teicher et al., 2000), with comorbidity affecting the expression of the disorder. Given equivocal results from previous imaging studies (Hendren et al., 2000), it is important to continue to investigate structural abnormalities in the putamen to understand its role in ADHD symptomolgy of inattention and hyperactivity. Finally, this study, along with the results from Pineda et al. (2002), suggests that comorbidity may have a significant impact on the neurobiology of disorders. Given that here is a high rate of comorbidity occurring with ADHD, this is an aspect that deserves further investigation to better understand children with neuropsychological disorders.

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**Tasha McMahon Wellington** is a doctoral student in the Department of Psychology at the University of Texas, Austin. She received her master's in clinical psychology from the University of Texas, Austin, and her master's in physiological science from UCLA. Her research interests are the neurobiology of developmental disorders.

**Margaret Semrud-Clikeman**, PhD, received her doctorate from the University of Georgia in 1990. She has published more than 30 articles, 40 chapters, and 3 books. She is currently a professor at the University of Texas at Austin and program director of the school psychology program.

**Amanda Louise Gregory** has her BA in psychology and communication arts from the University of Wisconsin, Madison, and her PhD in clinical psychology from the University of Texas at Austin. She is in private practice in San Francisco as a neuropsychologist. Research interests include the neuropsychology of antisocial behavior and the neuropsychology of emotion processing.

**Jennifer Mary Murphy**, PhD, is a clinical neuropsychologist in the Department of Neurology at the University of California, San Francisco (UCSF), holding the title of clinical instructor. Her research interests include comorbidity of frontotemporal dementia and ALS, emotion processing and the amygdala, and brain-behavior relationships in psychopathy.

**Jack Lynn Lancaster** is a research professor and head of the Biomedical Image Analysis Division at the Research Imaging Center, the University of Texas Health Science Center at San Antonio. His PhD is in Medical Physics and his research interests are in data modeling using measurements made by Magnetic Resonance Imaging, Positron Emission Tomography, and Transcranial Magnetic Stimulation. He also teaches graduate level courses in Medical Imaging to both medical Physics and Biomedical Engineering students.