

Diffusion Tensor Imaging of Pedophilia

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Abstract Pedophilia is a principal motivator of child molestation, incurring great emotional and financial burdens on victims and society. Even among pedophiles who never commit any offense, the condition requires lifelong suppression and control. Previous comparison using voxel-based morphometry (VBM) of MR images from a large sample of pedophiles and controls revealed group differences in white matter. The present study therefore sought to verify and characterize white matter involvement using diffusion tensor imaging (DTI), which better captures the microstructure of white matter than does VBM. Pedophilic sex offenders ($n = 24$) were compared with healthy, age-matched controls with no criminal record and no indication of pedophilia ($n = 32$). White matter microstructure was analyzed with Tract-Based Spatial

Statistics, and the trajectories of implicated fiber bundles were identified by probabilistic tractography. Groups showed significant, highly focused differences in DTI parameters which related to participants' genital responses to sexual depictions of children, but not to measures of psychopathy or to childhood histories of physical abuse, sexual abuse, or neglect. Some previously reported gray matter differences were suggested under highly liberal statistical conditions ($p_{\text{uncorrected}} < .005$), but did not survive ordinary statistical correction (whole brain per voxel false discovery rate of 5 %). These results confirm that pedophilia is characterized by neuroanatomical differences in white matter microstructure, over and above any neural characteristics attributable to psychopathy and childhood adversity, which show neuroanatomic footprints of their own. Although some gray matter structures were implicated previously, only few have emerged reliably.

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Introduction

Pedophilia refers to the sexual preference for children and poses a primary motivator for child molestation, which can incur great emotional and financial burdens on victims and on society, as well as on the pedophilic individuals themselves (Seto, 2008; World Health Organization, 2008). In some contexts, the sexual interest in children has been divided into the interest in specifically pre-pubescent children and that in specifically pubescent children—respectively termed *pedophilia* and *hebephilia* (Cantor & Sutton, 2014).¹ Clinical and forensic assessment research continues to

¹ In this article, we use the term pedophilia broadly, so as to include hebephilia. This corresponds to the ICD-10 definition: “A sexual preference for children, boys or girls or both, usually of prepubertal or early pubertal age” (World Health Organization, 2008).

improve our capacity to predict and thereby prevent recidivist behavior among sexual offenders against children (tertiary prevention); however, research on the etiology of pedophilia may yield opportunities for primary prevention, intervening even before the first sexual offense occurs.

Pedophilia has been associated with multiple etiologically relevant correlates, collectively suggesting it has a biological and potentially prenatal etiology: Relative to controls, pedophiles manifest lower mean IQs, poorer visuospatial and verbal memory test scores, lesser educational attainment, lesser physical height, an elevated propensity to have suffered head injuries before (but not after) age 13, atypical body morphology, and a rate of non-right-handedness up to three times population rates, similar to those observed in autism and mental retardation (Blanchard et al., 2002, 2003, 2007; Cantor et al., 2004; Cantor, Blanchard, Robichaud, & Christensen, 2005a; Cantor et al., 2005b, 2006, 2007; Dyshniku, Murray, Fazio, Lykins, & Cantor, 2014; Fazio & Cantor, 2015; Fazio, Dyshniku, Lykins, & Cantor, 2014; Fazio, Lykins, & Cantor, 2014; McPhail & Cantor, 2015). Although these findings do not necessarily rule out potential influences learned from the environment, it is virtually impossible to explain this pattern of findings without reference to prenatal, biological events.

Four pedophilic samples have been characterized with MRI thus far; however, these studies have varied in the types of pedophilic samples (high-risk, long-term incarcerates versus low-risk, community-dwelling pedophiles) and in the types of control samples (persons who committed nonsexual crimes versus persons with no criminal history), potentially confounding brain differences attributable to pedophilia with those attributable to confounds such as general criminality or psychopathy. Moreover, several studies employed small samples in combination with very liberal statistical thresholds, elevating the risk of both false positive and false negative results.

Schiltz et al. (2007) applied voxel-based morphometry (VBM) analyses to T₁-weighted anatomical scans, comparing 15 forensic inpatient pedophiles with 15 healthy community volunteers on a preselected set of brain regions, employing a liberal statistical threshold and found significant group differences in the right amygdala, hypothalamus, and bed nucleus of the stria terminalis. Those researchers also performed a whole-brain analysis, finding no region to differ at a more conservative, but still liberal threshold ($p_{\text{uncorrected}} < .001$). Concurrently, Schiffer et al. (2007) compared 18 high-security forensic inpatient pedophiles with 24 healthy community controls on a preselected—but entirely different—set of brain regions, again employing a liberal statistical threshold, finding 17 clusters to distinguish the groups. They also explored other brain regions with a more conservative threshold, finding no additional clusters. Although these two studies might seem to contradict each other, such a comparison would not be warranted: Both studies employed their most liberal threshold to test the regions they hypothesized (amygdala and diencephalic regions in the case of Schiltz et al. and frontostriatal and related regions in the case of Schiffer et al.) but more conservative (i.e., less sensitive) statistics

otherwise. Thus, the inconsistency might not reflect a failure to replicate, but reflect the uneven distribution of statistical power. An unbiased analysis would employ the same statistical threshold throughout the entire brain.

Cantor et al. (2008) conducted such an unbiased, whole-brain VBM analysis of T₁-weighted images, using a more conservative statistical threshold (corrected to a whole brain per voxel False Discovery Rate, or FDR, of 5 %) to compare a total of 65 low-risk outpatient pedophiles with 62 controls who had committed nonsexual offenses and were living in the community. Those procedures identified no significant group differences in any of the regions implicated either by Schiltz et al. or by Schiffer et al. Indeed, no group differences were significant at that level anywhere in gray matter; rather, the comparisons identified significant, wide-ranging differences in white matter. Because the aforementioned set of gray matter regions—including the hypothalamus, striatum, amygdala, and orbitofrontal (or inferior frontal) cortex, and cerebellum—have also been associated with psychopathy (Anderson & Kiehl, 2012; Blair, 2003; Kiehl et al., 2001; Müller et al., 2003; Soderstrom et al., 2002; Tiihonen et al., 2000; van Honk & Schutter, 2006), Cantor et al. hypothesized that the gray matter findings might be reflecting the criminality of the samples rather than their pedophilia.

Most recently, Poepl et al. (2013) compared nine pedophiles from high-security forensic hospitals with 11 nonsexual offender controls recruited from the same high-security forensic hospitals, applying a liberal statistical threshold to the regions previously implicated either by Schiltz et al. or by Schiffer et al. Poepl et al. then explored gray matter elsewhere in the brain, applying a more conservative statistical threshold (white matter regions were not investigated). Of the three regions implicated by Schiltz et al., Poepl et al. found a difference in one (amygdala gray matter decrease), and of the 17 regions implicated by Schiffer et al., Poepl et al. found a difference in one (insula gray matter decrease). At the more conservative threshold, three new regions emerged: dorsolateral prefrontal cortex, orbitofrontal cortex, and the angular gyrus. (Note, however, that the region Poepl et al. labeled *orbitofrontal cortex* may be the same region that Schiffer et al. labeled *inferior frontal gyrus*.)

Thus, (1) there is evidence suggesting an association between pedophilia and white matter, but no attempt to verify it or to measure white matter microstructure has yet been reported. (2) There has been evidence of differences between pedophilic and nonpedophilic samples in certain gray matter regions, but it remains unclear to what extent this might reflect a confound of psychopathy or of having experienced abuse in childhood, or be artifacts of small samples and liberal statistical thresholds. (3) Although there have been some attempts to approximate the criminality/psychopathy inherent to forensic samples of pedophiles by comparing them with forensic controls, no study has directly measured those features to account for them directly.

The present investigation sought to clarify the associations among pedophilia, its associated features, and brain structure.

To verify the presence of group differences, a new sample underwent an imaging technique better attuned to white matter microstructure, diffusion tensor imaging (DTI). Whereas T_1 -weighted imaging (the technique used by the prior four studies) is sensitive to differences between gray matter, white matter, and cerebral spinal fluid (CSF) in a way that allows the production of anatomical maps, DTI is highly sensitive to the movement of water molecules, allowing more detailed analyses specifically of fibrous tissue, such as white matter (but not gray matter or CSF). When a water molecule can move equally unimpeded in any direction, such as in CSF, its movement is *isotropic*; however, when a water molecule is impeded in some directions more than in other directions, such as moving more easily along axons than across them, it is said to be *anisotropic*. The more densely packed the fibers, the greater the anisotropy (i.e., the greater the difference in how easily water molecules can move along with rather than across the tracts). Different neuropathologies manifest changes in different parameters of diffusion; thus, quantification of the fractional anisotropy (FA) at each voxel allows highly detailed, quantitative assessment of the microstructural integrity of the underlying tissue.

To verify the presence of gray matter differences, T_1 -weighted anatomical scans were analyzed with a range of statistical thresholds, allowing direct comparison across existing reports. In addition, instead of employing a control sample of forensic patients to approximate levels of psychopathy and childhood adversity in the pedophilic sample, a nonforensic sample of healthy controls was examined, with psychopathy and childhood adversity quantitatively assessed to allow for independent analyses of which brain regions were associated with which feature.

Method

Participants

Sexual offender participants were recruited from the Kurt Freund Laboratory of CAMH, which provides evaluation services to male patients referred as a result of illegal or clinically significant sexual behaviors or interests. The primary source of referrals to the facility is parole or probation officers, with physicians and lawyers providing others. A patient was deemed eligible if he showed a phallometric response (described below) to any category of child (i.e., either pubescent or prepubescent; either male or female) that was greater than his responses to both categories of adults (i.e., men or women) and if he had committed one or more sexual offenses against a child 14 years of age or younger but no sexual offenses against any person age 17 or older. Because possession of child pornography is an even stronger predictor of pedophilia than is the direct commission of sexual offenses against children (Seto, 2013; Seto, Cantor, & Blanchard, 2006), charges for and admissions to such possession were treated as offenses

against children age 14 or younger. Controls were recruited from an online bulletin board, www.craigslist.org. Prospective participants for either group were excluded if they were younger than 18 years, were older than 60 years, weighed more than 300 pounds, had ever grinded metal, had metal in the eye, had metallic implants in the body, had a history of stroke or seizures, experienced claustrophobia, had a diagnosis of schizophrenia or bipolar disorder, or had history of a traumatic brain injury.

Procedure

Psychometry

Participants underwent a brief neuropsychological battery that included the Shipley Institute of Living Scales (Shipley, 1940) to estimate IQ, Edinburgh Handedness Inventory (Oldfield, 1971; Williams, 1986), and questionnaires for current and lifetime drug use and for histories of head trauma or neurological disease. The psychometric battery included a modified version of the Conflict Tactics Scale (CTS; Straus, 1979, as modified by Widom, personal communication, 2009) to assess experiences of violence in childhood, the Self-Reported Childhood Abuse—Physical scale (SRCAP; Widom & Shepard, 1996), the Childhood Neglect Index (Weeks & Widom, 1998), the Widom Child Sexual Abuse Interview (Widom & Morris, 1997), the Levenson Psychopathy Scale (LPS; Levenson, Kiehl, & Fitzpatrick, 1995), the CAGE alcohol use screening instrument (Ewing, 1984), and the Structured Clinical Interview for DSM-IV Axis I and II Disorders (SCID I and II; First, Gibbon, Spitzer, Williams, & Benjamin, 1997; First, Spitzer, Gibbon, & Williams, 2002).

Phallometry

The phallometric procedure was detailed by Blanchard, Klassen, Dickey, Kuban, and Blak (2001) and Blanchard et al. (2007). Briefly, a computer records a participant's penile blood volume while he is exposed to a standardized set of stimuli that depict a variety of activities and persons of potential erotic interest. Changes in penile blood volume (i.e., degree of penile erection) indicate the participant's relative erotic interest in each class of stimuli. The stimuli were audiotaped narratives presented through headphones and accompanied by slides. There were seven categories of narrative, depicting sexual interactions with females (either prepubescent, pubescent, or adult) or males (either prepubescent, pubescent, or adult), or solitary, nonsexual activities. The accompanying slides depict nude models corresponding in age and sex to the topic of the narrative (or landscapes, for the neutral narratives). The data reduction process yields seven category scores, one to reflect each of the six combinations of the age group and sex of the stimuli plus the neutral category. Finally, a Phallometric Pedophilia Index (PPI) was calculated as the sum of the responses to the child categories minus the sum to the adult categories. Thus, greater PPI scores represent greater pedophilia.

Image Acquisition

A 3T Signa HDx MRI system (GE Medical Systems, Milwaukee, WI), fitted with a standard 8-channel phased-array head coil, was used to obtain all images. For anatomical images, a T₁-weighted 3D inversion recovery (IR)-prepared FSPGR sequence (flip angle = 20°, TE = 5.12 ms, TR = 12 ms, TI = 300 ms) was used to generate 160 axial slices 1 mm thick (256 × 256 matrix, FoV = 20 cm²).

Diffusion-weighted data for each participant were acquired using a diffusion-weighted spin-echo single-shot echo-planar imaging sequence with diffusion encoding in 25 noncollinear directions ($b = 1000 \text{ s/mm}^2$) with 1 nondiffusion weighted reference volume ($b = 0 \text{ s/mm}^2$). The total diffusion-weighted image acquisition time was 324 s. The sequence parameters were: TR = 12 s; TE = 84 ms; matrix = 128 × 128; FoV = 30 cm²; 2.4 mm isotropic voxels.

Voxel-Based Morphometry

VBM analysis was performed with Statistical Parametric Mapping v8 (SPM8; Wellcome Trust Centre for Neuroimaging, London, UK) using all default options. In SPM8, spatial normalization, segmentation, and modulation are processed simultaneously using a unified segmentation algorithm (Ashburner & Friston, 2005). Anatomical T₁-weighted MR images were segmented into gray matter, white matter, and CSF classifications based on voxel intensity by an automated procedure. The segmented and modulated normalized images were smoothed with an isotropic 8 mm full-width-half-maximum filter.

Group comparisons were conducted using a two-sample *t* test with an absolute threshold of 0.05 and with total intracranial volume and age as covariates of no interest. To ascertain whether any gray matter differences reflected pedophilia or another feature, correlations were also calculated for the PPI, LPS, and CTS, using the whole sample (i.e., by combining groups). Whole brain data were analyzed using thresholds of: $p_{\text{uncorrected}} < 0.005$ ($t = 2.67$), $p_{\text{uncorrected}} < 0.001$ ($t = 3.26$), and FDR of 5 %, with a cluster extent threshold of 50. Areas of significant difference were localized using the SPM Anatomy Toolbox (Eickhoff et al., 2005) and the Harvard-Oxford Cortical Atlas (available within FSL v4.1 http://www.cma.mgh.harvard.edu/fsl_atlas.html).

Diffusion Tensor Imaging Analysis

Diffusion data were preprocessed using the Oxford Centre for Functional MRI of the Brain's (FMRIB's) software library (FSL v4.1.8, www.fmrib.ox.ac.uk/fsl) which included eddy current and motion artifact correction using the FSL Diffusion Toolbox (FDT; Leemans & Jones, 2009). Then, individual brain masks were created using the Brain Extraction Tool (Smith, 2002). FA values were calculated for each by fitting a tensor

model to the raw diffusion data using FDT. The remainder of the steps are part of the Tract-Based Spatial Statistics pipeline (TBSS, implemented in FSL; Smith et al., 2006). In brief, all participants' FA data were aligned into standard space (FMRIB 58_FA, available in FSL), using the nonlinear registration tool (FNIRT; Andersson, Jenkinson, & Smith, 2007a, 2007b), which uses a b-spline representation of the registration warp field (Rueckert, 1999). Next, the mean FA image was created and thinned to create a mean FA skeleton, representing the centers of all tracts common to the group. Each participant's aligned FA data were then projected onto this skeleton. Voxel-wise statistical analysis of the FA data was carried out using the randomize toolbox in FSL. Group comparisons were performed using nonparametric inferential statistics (5000 permutations) with cluster mass of $p_{\text{corrected}} = 0.025$ (Hayasaka & Nichols, 2003). Although the more liberal value of .05 is more typical in MRI research, much of the neuroimaging research on pedophilia employed highly liberal thresholds, yielding contradictory results. We therefore chose a more conservative value for the present analyses. Age was included as a covariate of no interest.

To ascertain whether white matter microstructure differences reflected the group differences in pedophilia or some other characteristic, a non-FA TBSS was performed for the principle parameters: axial diffusivity (AD), radial diffusivity (RD), mean diffusivity (MD), and mode (MO). Whereas routine, Cartesian geometry is expressed in X, Y, and Z (for length, width, and height), DTI employs polar geometry, using the direction of the fiber as the central axis. Thus, AD reflects water movement along a fiber, RD reflects water movement across (perpendicular to) the axis, MD reflects the overall amount of diffusivity in all directions, and MO reflects the departure from spherical movement (as either more planar or more cylindrical) from the origin (Moayed et al., 2012; Whitford, Kubicki, & Shenton, 2011). Values for each of these indices were extracted from the volume of interest by using the significant FA cluster as a mask. The associations between those indices and the behavioral/psychometric measures were then analyzed as zero-order correlations conducted on the full sample (both groups combined).

Probabilistic Tractography

The structural white matter connectivity of the regions showing group differences in white matter integrity was assessed with probabilistic tractography (FDT, part of FSL). A multifiber diffusion model that estimates the probability distributions of the direction of fiber populations was fitted at each seed voxel: The seeds were those voxels that showed significant FA differences between the pedophilic and control groups. Probabilistic diffusion tractography, estimates the probability of each voxel in the brain being an endpoint to a pathway passing through a seed voxel. To generate probabilistic maps, 5000 individual streamlines were drawn for each seed voxel with a step length of

0.5 mm and a maximum step number of 2000. Curvature threshold was set at 0.2 (corresponding to a minimum angle of approximately $\pm 80^\circ$) to preclude implausible pathways and back-tracking of pathways. Individual participants' maps were added together to create the maps for each group.

Group maps of the participants' tracts from the TBSS seed were calculated to determine regions that have differential connectivity between groups. The anatomical differences were identified with multiple atlases, including the Johns Hopkins University White Matter Tractography Atlas, ICBM-DTI-81 WMAtlas (Mori, Wakana, Nagae-Poetscher, & van Zijl, 2005; Wakana et al., 2007), the Harvard-Oxford Cortical Atlas, and the Harvard-Oxford Subcortical Atlas (http://www.cma.mgh.harvard.edu/fsl_atlas.html) available within FSLView v3.1.

Quantitative Tractography

To quantify the tractographical results, we thresholded the group tracts at 50 % (half of the control and half of the pedophilic group), created binary masks of each result, and subtracted each mask from the other to qualitatively identify regions of difference (targets). To assess whether these qualitative differences were quantitatively different, we performed tractography between the FA cluster seed and each of the regions that were qualitatively different. Tractography calculated the number of connections between each seed voxel projecting to each voxel of the different targets, producing a *waypoint* total for each participant and target. Each waypoint represents one connection between seed and target, and waypoint counts were analyzed with parametric statistics, $p < 0.05$ (two-tailed).

Research Ethics

All procedures were approved by the Research Ethics Boards of each of the Centre for Addiction and Mental Health (CAMH; Toronto, Canada), the University Health Network (Toronto, Canada), and Ryerson University (Toronto, Canada).

Results

Completing the study were 24 individuals in the pedophilic group and 32 controls (demographic and psychometric characteristics in Table 1). Eighteen additional prospective participants were excluded under the aforementioned criteria (metallic implants in the body, etc.). As anticipated, individuals in the pedophilic group showed highly significantly greater responses on phalometric testing (PPI) to stimuli depicting children than did the control group. The pedophilic group also demonstrated significantly greater psychopathy (LPS) scores and reported greater frequencies of experiencing punitive childhood discipline (CTS), consistent with prior studies of pedophiles and child molesters.

VBM of Gray Matter

At the conservative threshold employed in our prior investigation (whole brain corrected to $FDR < .05$; Cantor et al., 2008), no significant group gray matter differences between pedophiles and controls emerged. The same comparison repeated with more liberal thresholds, however, implicated multiple structures potentially differing between the groups (Table 2). Using the entire sample (by combining groups), no significant correlations were identified by VBM between gray matter and the PPI, LPS, or CTS at the conservative threshold. At the most liberal threshold ($p_{uncorrected} < .005$), however, two gray matter regions significantly correlated negatively with PPI (right occipital gyrus [$X = 32, Y = -82, Z = -2$], 164 voxels; and right superior temporal gyrus [$X = 72, Y = -26, Z = 12$], 128 voxels), but no such region related to the LPS or CTS.

Microstructural Analysis of White Matter

TBSS identified a significant group difference in FA, localized to a discrete, 288-voxel cluster of white matter of the left hemisphere (MNI coordinates: peak [$X = -22, Y = 27, Z = -4$], center of gravity [$X = -24, Y = 15.2, Z = 12.2$]), identifying this cluster as our volume of interest (Fig. 1). Neuroanatomically, this is a highly complicated region, through which pass multiple fiber tracts, including the internal and external capsules, the corona radiata, the inferior fronto-occipital fasciculus, and the anterior thalamic radiation. FA across the cluster was significantly elevated in the pedophilic group, $t(54) = 5.13, p = .000004$, as was mode, $t(54) = 2.44, p = .018$. These parameters reflected significantly greater axial diffusivity, $t(54) = 2.67, p = .010$ and significantly lower radial diffusivity, $t(54) = -4.37, p = .000058$, but without a significant difference in medial diffusivity, $t(54) = 1.37, p = .18$.

To ascertain whether the microstructural features of this volume were associated with pedophilia or with one of the other group differences, the correlations between the DTI parameters and other sample characteristics were calculated (Table 3). Although FA significantly correlated with penile responsivity to erotic depictions of children, no significant correlations were found between FA and the measures of psychopathy or childhood sexual abuse, violent abuse, or neglect. Significant associations of FA were detected, however, with alcohol use, educational attainment, and self-reporting of ever having been bothered sexually (in one's lifetime, not necessarily during childhood). Although the pedophilic and control groups differed in CTS scores, this measure was not significantly associated with FA in the volume of interest. The correlations between behavioral characteristics and the individual diffusivity indices demonstrated that although four behavioral variables were associated with FA, each such variable showed a distinct pattern in diffusivity: While PPI was associated with greater axial diffusivity and lesser radial diffusivity, education was associated with lesser diffusivity on both the axial and radial parameters, and alcohol use significantly related to (lesser)

Table 1 Demographic, psychometric, and behavioral characteristics of pedophilic and control groups

Characteristic	Pedophiles	Controls	Comparison
Demographic and cognitive			
Mean age in years (SD)	35.63 (9.52)	37.00 (10.72)	$t(54) = .50, p = .621$
Estimated IQ (SD)	100.90 (13.38)	103.53 (10.94)	$t(47) = -0.14, p = .892$
Education, in years (SD)	12.64 (2.30)	15.25 (9.52)	$t(51) = 4.06, p = .00017$
Non-right-handed, percent	19.0 %	9.3 %	$\chi^2(1) = 1.04, p = .309$
Sexological			
Phallometric pedophilia index (SD)	1.62 (1.36)	-1.50 (1.07)	$t(54) = 9.60, p < .00001$
Admit pedophilia, percent	33.3 %	0 %	*
Homosexual, percent	16.67 %	18.75 %	$\chi^2(1) = 0.028, p = .866$
Number of victims younger than age 11 (SD)	4.5 (6.78)	0	*
Number of victims ages 11–14 (SD)	1.33 (0.58)	0	*
Committed 1+ child pornography offences, percent	62.5 %	0 %	*
Childhood adversity			
Conflict Tactics Scale (SD)	23.37 (17.07)	13.46 (8.40)	$t(44) = 2.65, p = .011$
Self-Reported Childhood Abuse—Physical (SD)	1.25 (1.74)	1.13 (1.26)	$t(50) = 0.30, p = .766$
Widom Childhood Sexual Abuse Index (SD)	3.30 (3.90)	2.53 (3.12)	$t(50) = 0.78, p = .437$
Childhood Neglect Index (SD)	0.70 (1.21)	0.28 (0.52)	$t(23.433) = 1.46, p = .159^{**}$
“Consider these experiences sexual abuse?”, percent yes	25.0 %	12.5 %	$\chi^2(1) = 1.46, p = .227$
“Been bothered sexually ever in life?”, percent yes	45.0 %	12.5 %	$\chi^2(1) = 6.93, p = .008$
Personality and psychiatric			
Levenson Psychopathy Scale (SD)	51.15 (12.97)	44.72 (8.45)	$t(50) = 2.17, p = .035$
CAGE (SD)	1.06 (1.43)	0.45 (0.96)	$t(45) = 1.74, p = .089$
SCID Axis I, number meeting criteria			
Current major depression	7	10	$\chi^2(1) = 0.08, p = .779$
Lifetime major depression	9	10	$\chi^2(1) = 1.00, p = .317$
Current and lifetime dysthymia	1	3	*
Lifetime general anxiety disorder	0	1	*
Lifetime panic disorder	2	3	*
Lifetime simple phobia	1	0	*
Lifetime OCD	2	0	*
Lifetime PTSD	0	2	*
Lifetime any eating disorder	2	2	*
Lifetime binge eating	1	1	*
SCID Axis II, number meeting criteria			
Current and lifetime paranoid	1	1	*
Current and lifetime borderline	1	0	*
Current and lifetime antisocial	2	0	*
Current and lifetime avoidant	2	0	*
Current and lifetime dependent	1	0	*
Current and Lifetime obsessive–compulsive	1	1	*
Current and lifetime passive-aggressive	0	2	*
Current and lifetime depressive	1	1	*

* Comparison obviated where cell counts are fewer than five. ** Comparison failed Levene's Test of equal variances at $p < .05$; degrees of freedom and significance values adjusted to reflect t -test for unequal variances

radial diffusivity only. Although the self-reported experience of ever having been bothered sexually (lifetime) showed a small association with FA, it was not significantly related to any of the diffusivity indices.

Probabilistic Tractography

Figure 2a, b show the trajectories of the tracts from the region with significantly different FA between the pedophilic and

Table 2 Regional gray matter volume decreases in pedophilic versus control group at liberal versus conservative thresholds

Brain region	X	Y	Z	Clusters at $p_{\text{uncorrected}} < .005$	Clusters at $p_{\text{uncorrected}} < .001$	Clusters at FDR < .05*
L cerebellum (VIIa)/visual cortex	-36	-86	-8	907		
L superior temporal gyrus	-72	-20	10	785	64, 63**	
R visual cortex	10	-96	28	458		
R superior temporal gyrus	72	-8	-2	453	100	
L cerebellum (VIIb)	-22	-78	-56	413		
R cerebellum (VIIb)	38	-74	-60	385		
R cerebellum (VIIa)	20	-30	-42	343		
L hippocampus	8	-6	-32	340		
R precentral gyrus	56	-12	60	298		
L&R orbitofrontal cortex	-6	44	-32	279		
R inferior temporal gyrus	72	-40	-18	236	56	
L premotor cortex	-6	18	74	189		
R occipital gyrus	28	-80	0	177		
L cerebellum	-36	-42	-60	163		
R frontal pole	36	66	-6	150		
L occipital gyrus	-36	-78	4	134		
L inferior temporal gyrus	-68	-20	-28	131		
L temporal pole	-48	4	-48	98		
L inferior parietal lobule	-68	-22	42	97		
L frontal pole	-32	60	-20	94		
R medial temporal pole	46	16	-44	88		
L inferior parietal lobule	-50	-76	30	81		
R superior parietal lobule	16	-66	72	77		
L superior parietal lobule	-42	-46	62	74		
L postcentral gyrus	-54	-14	58	71		
R temporal pole	64	8	-10	70		
R primary somatosensory cortex	36	-34	74	68		
R frontal pole	26	64	24	66		
L DLPFC	-32	42	48	63		
R supramarginal gyrus	72	-30	34	57		

MNI Montreal Neurological Institute, L left, R right

* No cluster was significant at FDR < 0.05; ** Second cluster is at [-68, -6, -4]

control groups. The difference in FA is associated with tracts in the pedophilic group that were less connected to the insula/operculum/temporal pole/superior temporal gyrus, $t(54) = -2.35$, $p = .022$; occipital cortex, $t(54) = -3.53$, $p = .001$; dorsolateral prefrontal cortex (DLPFC), $t(54) = -2.29$, $p = .028$; temporo-occipital junction, $t(54) = -2.18$, $p = .033$; and superior parietal lobule, $t(54) = -2.27$, $p = .028$, in the left hemisphere. Regions *more* connected among the pedophilic group (Fig. 2c, d) were the thalamus, $t(54) = 2.82$, $p = .009$; and the frontal pole, $t(54) = 3.46$, $p = .002$. The correlations between the behavioral characteristics and the brain regions with atypical connectivity to the volume of interest appear in Table 4.

Discussion

The present study provided more precise characterization of cerebral white matter among pedophiles. In prior MRI studies of pedophilia, white matter was either unexamined (in the case of Poepl et al., 2013) or, because no differences were predicted, was examined with substantially less statistical power than were gray matter structures (in the cases of Schiffer et al., 2007 and Schiltz et al., 2007). Regarding gray matter differences, when applying the same (conservative) statistical threshold in Cantor et al. (2008), we attained the same result as our original study: no significant gray matter differences. When repeating those analyses with a more liberal statistical threshold, more

Fig. 1 Group differences in fractional anisotropy (FA) between pedophilic and control groups. *Red/yellow* regions indicate significant increases in FA in the pedophilic group relative to controls using nonparametric permutation testing (corrected for multiple comparisons with cluster-mass correction, $p \leq 0.025$) and overlaid on the white matter skeleton (*green*). Significant clusters have been thickened using *tbss_fill* for enhanced visualization

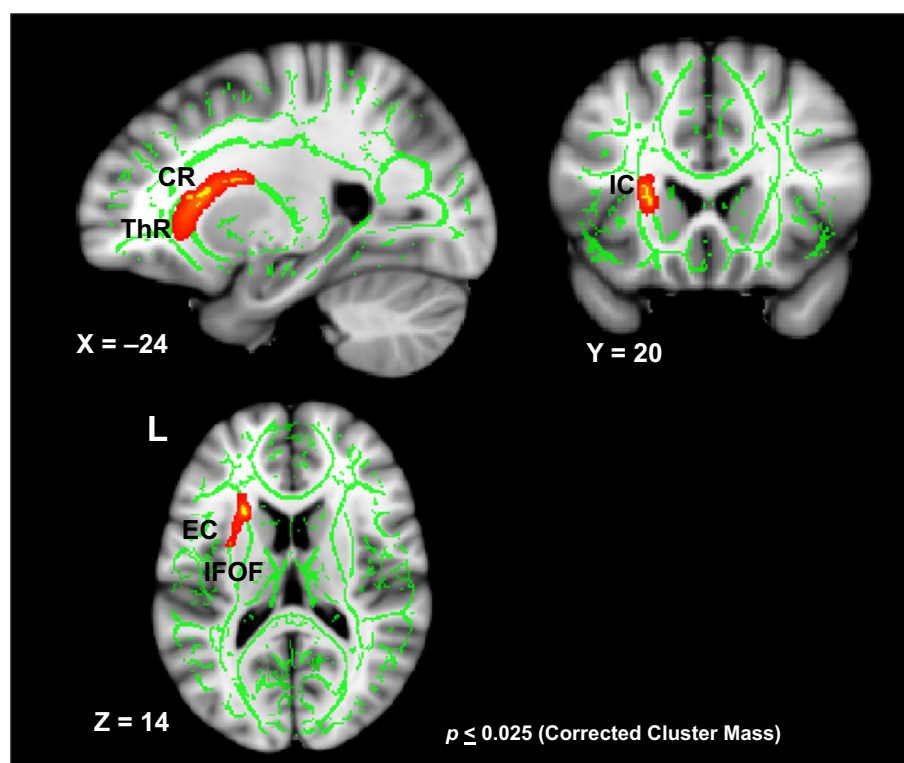


Table 3 Correlations of behavioral characteristics with fractional anisotropy and diffusivity in identified volume of interest

Characteristic	FA	MO	AD	MD	RD
Age ($n = 56$)	.01	.25	.08	.02	-.01
Years of education ($n = 53$)	-.44***	-.31*	-.38**	-.01	-.39*
IQ ($n = 49$)	.09	.16	.06	-.02	-.07
Levenson Psychopathy Scale ($n = 52$)	.14	.14	.17	.08	-.06
Conflicts Tactics Scale ($n = 46$)	.06	-.13	.08	.06	.01
Widom Childhood Neglect Index ($n = 52$)	-.05	-.08	-.02	.02	.04
Phallometric Pedophilia Index ($n = 56$)	.51****	.17	.30*	-.17	-.45***
Widom CSA Score ($n = 52$)	.01	.08	.12	.17	.09
Sexual Abuse? ($n = 56$)	.15	.15	.16	.05	-.09
Ever bothered sexually? ($n = 52$)	.29*	.12	.18	-.05	-.23
Self reported childhood abuse score ($n = 52$)	.05	.04	.18	.18	.04
CAGE ($n = 47$)	.42**	.14	.24	-.14	-.37*

* $p < .05$ (two-tailed); ** $p < .01$ (two-tailed); *** $p < .001$ (two-tailed); **** $p < .0001$ (two-tailed)

comparable to that employed by the other studies, we attained the same result as the other studies: group differences in several gray matter structures. Indeed, the set of gray matter regions implicated here (with low-threshold statistics) overlapped with the Schiffer et al. (2007) and the Schiltz et al. (2007) results even more strongly than did the explicit effort by Poepl et al. (2013) to replicate those gray matter findings (see below). The seeming inconsistencies among studies of gray matter in pedophilia appear to be attributable to differences in statistical power.

No individual study has had sufficient statistical power to identify gray matter regions that differentiate pedophilic and nonpedophilic groups at a conservative threshold. Nonetheless, some tentative hypotheses might be offered regarding regions that have been implicated at liberal thresholds. One region has been identified in three studies: orbitofrontal cortex (present report plus Poepl et al., 2013; Schiffer et al., 2007), and five regions have been implicated in two studies: insula (Poepl et al., 2013; Schiffer et al., 2007), superior temporal gyrus (present report plus Schiffer et al., 2007), middle temporal gyrus or

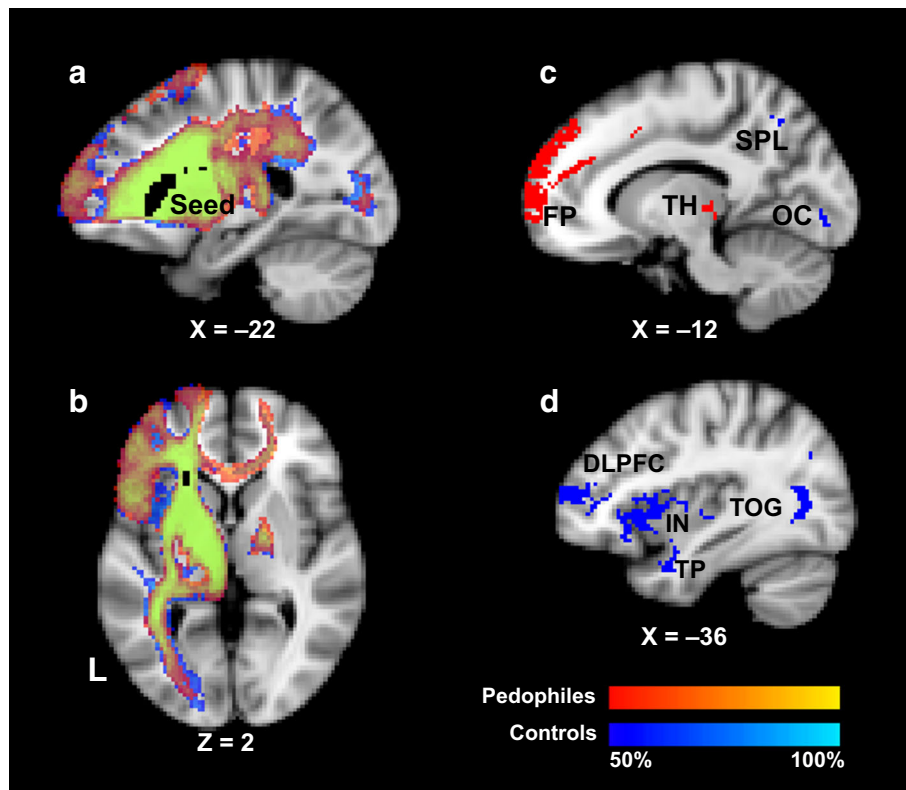


Fig. 2 Qualitative probabilistic tractography for the tract-based spatial statistics (TBSS) cluster result. Seed voxels appear in *black* (**a**, **b**) and reveal that the abnormal white matter region has different connections in pedophiles and controls. To quantify the observed qualitative differences, we performed a second tractographic analysis from the TBSS seed to the specified targets based on the observed differences. *Blue* indicates trajectories reached significantly less probably by the pedophilic group, *red* indicates trajectories reached significantly more probably by the

pedophilic group, and *yellow* indicates overlapping trajectories. Quantitative tractography (**c**, **d**) revealed that more voxels from the seed region project to the left frontal pole (FP) and the left thalamus (TH) in the patients relative to controls (C). The pedophiles have a lower connection probability in between the seed region and the insula (IN), temporal pole (TP), superior temporal gyrus, operculum, occipital cortex (OC), dorsolateral prefrontal cortex (DLPFC), temporal–occipital junction (TOJ), and superior parietal lobule (SPL), all unilateral left

Table 4 Correlations between behavioral characteristics and probability of connectivity with identified volume of interest

Characteristic	Left insula/operculum/ temporal pole/superior temporal G	Left occipital cortex	Left dorsolateral prefrontal cortex	Left temporal– occipital-junction	Left superior parietal lobule	Left frontal pole	Left thalamus
Years of education (<i>n</i> = 53)	.37**	.45***	-.04	.10	.22	-.27*	-.26*
Phallometric Pedophilia Index (PPI) (<i>n</i> = 56)	-.24*	-.26*	-.23*	-.18	-.06	.25*	.26*
Ever bothered sexually? (lifetime) (<i>n</i> = 52)	-.39**	-.36**	-.08	-.25*	-.11	.19	.08
Alcohol consumption (CAGE) (<i>n</i> = 47)	-.13	-.24	.07	.13	-.20	.11	.00

* $p < .05$ (two-tailed); ** $p < .01$ (two-tailed); *** $p < .001$ (one-tailed)

temporal pole (present report plus Schiffer et al., 2007), amygdala (Poeppl et al., 2013; Schiltz et al., 2007), and cerebellum (present report plus Schiffer et al., 2007).

Because DTI provides greater information about white matter structure and microstructure than do T_1 -weighted images, the present results can provide more accurate information about the location and connectivity of the white matter that distinguishes the

pedophilic and control samples. Whereas Cantor et al. (2008), our initial investigation, implicated widespread white matter differences connecting multiple cortical regions, the present results implicated a region more focal in size, but involving multiple tracts that (as a set) connect those cortical regions. More specifically, probabilistic tractography identified the endpoints/sources of the group differences in connectivity to be: insula/operculum,

superior temporal gyrus, temporal pole, occipital cortex, dorso-lateral prefrontal cortex, temporal–occipital junction, superior parietal lobule, frontal pole, and thalamus (all unilateral left). Despite these gray matter regions being identified entirely empirically, they are remarkably similar to the regions identified by meta-analyses of functional neuroimaging studies to be those that most reliably respond to sexual stimuli (Kühn & Gallinat, 2011; Poepl, Langguth, Laird, & Eickhoff, 2014; Stoléru, Fonteille, Cornélis, Joyal, & Moulrier, 2012). Although tentative, the commonality between these lines of otherwise independent literatures suggests the gray matter endpoints as potentially important regions of interest for subsequent research.

In the present sample, penile responses to sexual depictions of children were strongly related to elevated FA but not to mode of the white matter region. Although brain regions with crossing fiber tracts can manifest complicated geometries, the simplest anatomical cause of increased FA and unaffected modal diffusivity is thinner tracts, such as would be exhibited by lesser myelination (increasing how densely packed axons are with each other) or by a deficiency in the number of axons composing the tract (Whitford et al., 2010). That is, in these circumstances, membranes are positioned more closely together (exaggerating the difference between diffusivity along rather than across the fiber) but without affecting the relative planar versus cylindrical shape in which water will move. Interestingly, penile responses to erotic depictions of children were not associated with a straightforward pattern of lesser connectivity between brain regions. Rather, it was associated with a pattern of significantly greater connectivity to some regions and significantly lesser with others (Table 4). This suggests a pattern of *dysconnectivity* rather than *disconnectivity*. Although the DTI and other methods employed in this study are not sufficient by themselves to guarantee that conclusion, the present results suggest that future investigations explore not only an absence of expectable connectivity (perhaps decreasing sexual responses towards adults), but also the presence of unusual connectivity (increasing sexual responses towards children).

The white matter differences detected here were not readily attributed to psychopathy or experiences of childhood adversity: The groups did not differ significantly on the measures of childhood neglect or sexual abuse, and, although the groups did differ on psychopathy and punitive childhood punishments, those characteristics were not significantly related to any of the anisotropy or diffusivity measures in the volume of interest. Thus, although those characteristics may have neural correlates of their own, they do not appear to explain the group differences detected here.

Although psychopathy and childhood adversity were hypothesized to be potential confounds for the neural correlates of pedophilia, it was a subset of the routine, demographic variables that instead showed significant associations with FA in the volume of interest (and therefore merit investigation as potential confounds): educational attainment, alcohol use, and reporting having been bothered sexually any time during life. As did pedophilia, lesser education predicted elevated FA in the volume

of interest; however, the educational differences did not explain the diffusivity pattern for pedophilia. Whereas pedophilia related to greater axial diffusivity and lesser radial diffusivity, education related to lesser diffusivity in both directions. This suggests that both pedophilia and educational capacity relate to neuroanatomy, but that each has its own, dissociable neuroanatomic footprint. Interestingly, despite the differences in education between the samples, there was no significant difference in IQ between these groups. (Although lesser IQ is often reported in clinical forensic samples [Cantor et al., 2005a], those who volunteer to participate in research studies typically demonstrate higher IQ scores.) Alcohol use and participant responses to ever having been sexually bothered in their lives both demonstrated a set of associations with FA and diffusivity parameters similar to those shown by pedophilia (but lesser in magnitude). Despite the similarity between alcohol use and pedophilia on the DTI metrics, the pedophilic and nonpedophilic groups did not differ significantly from each other in terms of actual alcohol use. Moreover, in our prior MRI study comparing pedophiles with individuals who had committed nonsexual offenses, it was the nonsexual offenders who reported significantly greater rates of alcohol use.

PPI was associated with the connectivity of volume of interest with most of the identified regions. Whereas alcohol consumption (CAGE) scores showed FA and diffusivity characteristics similar to those of pedophilia, CAGE scores did not relate significantly to connectivity. Although self-report of having ever been bothered sexually (lifetime) related to increased FA and decreased connectivity to the same areas as with pedophilia, it did not show the corresponding increases in connectivity. Educational attainment, however, exhibited a similar (but inverse) connectivity pattern as with pedophilia.

Considered together, the characteristics provided by DTI metrics—FA, diffusivity, and connectivity—yielded a unique pattern of features that distinguish pedophilic from nonpedophilic individuals and from hypothesized and empirically derived potential confounds.

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