Widespread and interrelated gray matter reductions in child sexual offenders with and without pedophilia: Evidence from a multivariate structural MRI study

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Aim: To further investigate the neuroanatomical correlates of child sexual offending and disentangle them from the neural correlates of pedophilia, using a multivariate analytical approach in order to minimize loss of statistical power.

Methods: This study presents structural MRI data on gray matter in an incarcerated, male population of 22 pedophilic and 21 non-pedophilic child sexual offenders, and 20 violent non-sexual offender controls, based on a multivariate whole-brain approach using source-based morphometry.

Results: We identify a network of several neuroanatomical regions exhibiting interrelated reduced gray matter in both child sexual offender groups relative to controls, comprising extensive clusters in the bilateral cerebellum and frontal lobe, as well as smaller clusters in the bilateral parietal, temporal, and occipital lobes, the bilateral basal ganglia, the medial cingulate and the hippocampus.

Conclusion: Our results speak to the interpretation that there are inter- and possibly connectivity-related brain structural abnormalities in child sexual offenders that are not (only) pertaining to pedophilia per se. Interpretations and limitations of the present data are discussed and recommendations for future works are given.

Keywords: brain, child abuse, sexual, forensic psychiatry, MRI, pedophilia.

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Child sexual offending (CSO) is one of the gravest disturbances to a child’s life, often followed by severe disruptions to victims’ well-being and development.1,2 Approximately 11.8% of children become victims of CSO according to a 2011 international meta-analysis (N = 9,911,748).2 One central risk factor for CSO is pedophilia (P), a persistent or dominating sexual preference for prepubescent children, marked by recurrent sexual urges, fantasies, or behaviors involving sexual activity with a prepubescent child or children. According to the International Classification of Diseases (10th revision; ICD-103), this preference must prevail for at least 6 months and must be present in a person who is at least 16 years old and at least 5 years older than the child/children. Importantly, the person affected must either suffer from or have exhibited their sexual preference (F65.4). These criteria are fairly similar to a ‘pedophilic disorder’ in the 5th Diagnostic Statistical Manual (DSM-5 (302.2)).4 The DSM-5 however differentiates between this ‘pedophilic disorder’ and a ‘pedophilic sexual orientation’, i.e. the deviant preference in absence of its enactment, feelings of guilt, shame, or anxiety, and functional limitations due to the preference. This highlights that preference and behavior are not synonymous since, contrary to public belief, a pedophilic preference is present in only about 40–50% of child sexual offenders (CSOs).5 Various motivations for non-pedophiles to commit CSO have been proposed, including a lack of alternative partners, and psychopathology such as other paraphilias or antisociality. Conversely, their offenses have been found to be more opportunistic, violent, and non-exclusive to children.6–8 Both pedophilia and CSO have inspired considerable research, in which possible neural bases have been of special interest.

Until recently, the two phenomena have often remained cofounded, either by not clearly differentiating groups or by the use of only data from pedophilic offenders (+CSO-P), leaving out non-pedophilic offenders (+CSO-P) and pedophilic non-offenders (-CSO +P). In this literature, +CSO-P have been found to exhibit abnormalities regarding (prenatal) neurodevelopment markers,9–14 neuro-psychological performance15–18 and their neurofunction regarding various paradigms and connectivity.15,16,19–27 Structural gray matter reductions have been reported for regions in the frontal,28,29 parietal,28 and temporal lobe,28 including for limbic loci,29,30 as well as for the cingulate cortex,28 the insula,28,29 structures of the basal ganglia,28 and cerebellar loci.28 Therein, some of these exhibited correlations of gray matter with pedophilia-related markers, leading to the hypothesis that neuroanatomical disturbances in pedophilia may be dimensional rather than categorical.29 Simultaneously, multiple studies have reported no significant group differences in gray matter.
and some instead in white matter.31,32 This is in line with findings of
resting-state functional connectivity,24,25 and not necessarily contra-
dictory to former gray matter findings, as the structures connected by
significantly reduced white matter tracts overlap with structures found
to be abnormal in gray matter32 and previously identified abnormal
gray matter structures have been found to exhibit substantial intercon-
nectivity.31 However, the literature is heterogeneous regarding analyti-
cal approaches (thresholds, whole-brain or ROI analyses), control
groups (non-offenders or non-sexual offenders), and inclusion criteria
for +CSO+P groups (diagnoses, phallometric results, varying crimi-
nological properties, admission to preference, or a combination).

More recently, neuroscientific works have begun to disentangle P
and CSO, regarding executive functioning,25-29 IQ,30 behavioral
control,21 affect recognition,41 resting-state functional connectivity,42
and neurostructure.40,43 Schiffer et al.,43 (as part of the NeMUP
research initiative) conducted a whole-brain comparison of 58 +CSO+
and, 60 -CSO+P, and 101 non-pedophilic, non-offending controls
(please note that some studies, due to their psychiatric rather than
forensic focus, use the notation of P+CSO to describe pedophilic
CSOs, thereby putting P first; inclusion criteria may very slightly due
to prioritizing one before the other when building the sample). No
difference emerged between pedophiles and controls overall, but
+CSO+P exhibited lower gray matter volume relative to -CSO+P in
the right temporal pole. Lett et al.,30 also examined pedophilic men
with and without a history of CSO and again found (gray and white)
matter reductions in +CSO+P but not -CSO+P, in the right motor
cortex, the frontal and temporal lobe, and the corpus callosum, among
others.

Overall, it remains uncertain whether +CSO+P exhibit neuro-
structural abnormalities and which features any differences may be
related to, not least because data from +CSO-P are still missing. First
neuroanatomical data from -CSO+P and +CSO+P may indicate
CSO, rather than P, to be associated with neuronal anomalies, though
it remains possible that both phenomena exhibit their own (over-
lapping) neuropathology.46,43 Concurrently, both +CSO+P and
+CSO-P have been found to exhibit neuropsychological impairments,
though with stronger weaknesses in +CSO-P and differing executive
profiles.36-39

The present study contributes to ongoing efforts in neuroscience
to disentangle the phenomenology of CSO and P by presenting gray
matter data from incarcerated +CSO+P, +CSO-P, and non-sexual
violent offenders (NSOs). It is, to our knowledge, the first neuroana-
tomical study on CSOs to include +CSO-P subjects. Given the mixed
evidence thus far and hints of connectivity-related abnormalities, we
conducted a whole-brain analysis using a multivariate, data-driven
approach that allows for the identification of networks of neuroana-
tomical loci exhibiting interrelated abnormal gray matter volume.34

**Methods**

**Data collection and participants**

All data were taken from from the Kiehl lab data pool at the Mind
Research Network (MRN), collected between 2010 and 2014.15-47
The lab uses a Siemens mobile MRI scanner to collect neuroimaging
data in maximum-security detention facilities across the United
States, which has allowed for the analysis of large samples in the field
of forensic psychiatry. Subjects provide informed consent to the use
of their data in continued research prior to participation. All assess-
ments were ethically approved by The University of New Mexico
Institutional Review Board and are continually approved by Ethical
and Independent Review (E&I); the present study conforms to the
Declaration of Helsinki.

The data pool was searched for subjects who fit inclusion criteria
for this particular study. As the most reliable information was crimi-
nological, inclusion and subject allocation was primarily based on this
info supplemented by psychiatric information where possible and
applicable, and kept as conservative as possible to avoid misallocation
of (CSO) subjects, resulting in a moderate final sample size despite
the initially large data pool.

General inclusion criteria were an age between 18 and 65, a full-
scale IQ of or above 75, fluency in English, a 4th grade reading level
higher, no history of seizures in self or of psychotic disorder in self
or first-degree relative, as well as no mood disorder and no alcohol or
drug use at the time of assessment. All CSOs had offended against at
least one victim under 11 in a sexual offense. To be sorted into the
+CSO+P group, subjects had to have had hands-on sexual vic-
tims above the age of 16 and a DSM-IV-TR pedophilia diagnosis, for
which the criteria are the same as those for a pedophilic disorder in
the DSM-5.48 +CSO-P either had victims over 16 or no pedophilia
diagnosis. NSOs had committed at least one homicide, to hold con-
stant the factors of having committed a violent offense among sub-
jects, and no sexual offenses.

Information on subjects’ demographics, psychological, psychiatric
(including neurobiologically relevant medication at time of assess-
ment, i.e. neuroleptics, SSRIs, amphetamines, and antihistamines),
and criminological background was extracted from legal documents,
nickname files and, if available, psychiatric assessments. This informa-
tion had been assessed beforehand by MRN staff or by the incarcer-
ations institutions. IQ had been assessed using the Wechsler Adult
Intelligence Scale III49 and psychopathy had been assessed using the
Psychopathy Checklist-Revised50 (see former Kiehl lab publications
for more info). Crimes were summarized into the total number of all,
non-violent, and violent (sexual and non-sexual) crimes, both from
convictions and from self-reports.

**Imaging data**

All MRI scans were acquired with the MRN Siemens 1.5T Avanto
mobile scanner with a multi-echo MPRAGE pulse sequence (repeti-
tion time = 2530 ms, echo times = 1.64 ms, 3.50 ms, 5.36 ms, 7.22
ms, inversion time = 1100 ms, flip angle = 7°, slice thickness = 1.3 mm, matrix size = 256 x 256). This yielded 128 sagit-
ital slices with an in-plane resolution of 1.0 mm x 1.0 mm.

**Data analyses**

**Pre-processing of imaging data and SPM**

Imaging data were pre-processed using Statistical Parametric
Mapping 12 (SPM12, Wellcome Department of Cognitive Neurology,
London, UK; http://www.fil.ion.ucl.ac.uk/spm) and analyzed using
Source-Based Morphometry (SBM, performed using GIFT software,
available from TReNDS; https://trendscenter.org/software/).44 a multi-

ariable alternative to Voxel-Based Morphometry (VBM). Pre-
processing for SBM was done in the same manner as has been done
for VBM52; details of the procedure used with the present data can be
found in the Supplement. Using Independent Component Analysis
(ICA),52 SBM identifies patterns of voxels that show maximal covari-
ation regarding gray matter in the sample and maximal independence
from other networks of covariation. Its qualities and comparison to
VBM have been elaborated on before.52 Each network is captured in
one component. For the present work, the number of components was
set to 30, as in other studies using SBM.53 ICA is independent from
subjects’ group affiliation. It produces individual loading values that
represent the extent to which a given component contributes to each
subject’s T1 image. Loading values can therefore subsequently be
used for statistical group analyses. The final interpretation of group
differences is conditional on a component’s spatial image. Higher
loadings of predominantly positive components should be interpreted
as higher matter volume or density, whereas higher loadings of nega-
tive components stand for lower matter volume or density.

**Statistical group analyses**

All statistical group analyses were performed in RStudio version
3.5.1.22 Demographic, psychological and psychiatric, criminological,
and global morphological information was tested for group differ-
ences using one-way analysis of variance (ANOVA) or Kruskal-Wallis-

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tests for normally and non-normally distributed interval-scaled numeric data, respectively. For pairwise comparisons, independent samples *t*-tests and Mann–Whitney–U-tests were performed. For count data, *χ*²-tests were performed when expected frequencies exceeded five in all cells and Fisher’s exact tests were used when they did not.

**SBM component loadings**

Individual component loadings were entered into a multivariate analysis of variance (MANOVA) with group as the sole predictor and all 30 components as dependent variables (step 1). A significant MANOVA result can be interpreted as indication for a true, non-noise difference between groups in at least one dependent variable (in this case a component), but should be followed-up with an analysis of variance (ANOVA) for each dependent variable to determine in which one(s) the difference lies.

We therefore determined that following a significant MANOVA, we would compute a follow-up one-way ANOVA for every component, again with group as the sole predictor (step 2). If the ANOVA for a component exhibited a significant result (Holm-corrected *P* < 0.05), it would be followed up with (i) a linear model with relevant control variables as additional predictors; and (ii) pair-wise comparisons of the three groups using independent samples *t*-tests (step 3). If a component did not exhibit a significant group difference in step 2, we would refrain from further investigating them.

**Average gray matter in significant component clusters**

Since one component comprises multiple morphological structures, if any components were to exhibit a significant *P*-corrected ANOVA result (as indicated in step 2), they were decomposed into the clusters they encompassed, identified using probabilistic cytoarchitectonic maps in the Anatomy Toolbox 2.1 implemented in SPM8 (height threshold: *z* > 2, extend threshold: *k* = 2 voxels, http://www.fz-juelich.de/imn/imn-1/DE/Forschung/_docs/SPMAnatomyToolbox/SPMANatomyToolbox_node.html55–57) and the Brainnetome Atlas, a morphological parcellation atlas based on meta-analytic structural and functional connectivity data58 (please see Table S1 in the Supplement for Brainnetome regions and subregions). Then, individual average gray matter was extracted for 10 mm radius spheres surrounding the peak voxels of clusters exceeding 300 vox. On this data, steps 1, 2, and 3 were run again, to determine whether one or more clusters within components that were significantly different between groups drove this significance finding particularly.

**Neuroanatomical group differences**

Before each MANOVA analysis, general (multivariate) data distribution assumptions were examined. If data did not entirely fulfill these assumptions, an additional, rank-based MANOVA61,62 was computed.

**Results**

**Sample characteristics**

Out of approximately 300 screened subjects, a total of *N* = 63 was included in the final sample. Out of these, 22 subjects were entered as +CSO-P, 21 as +CSO-P, and 20 as NSOs. Available demographic, psychological, criminological, and global morphological information and group comparisons can be found in Table 1.

Group comparisons revealed significant differences in age, IQ, total number of crimes, violent crimes, non-sexual crimes, and in PCL-R scores (Table 1). More specifically, NSOs were younger and had committed less crimes overall than both CSO groups (though, per definition, at least one homicide). Among CSOs, +CSO-P exhibited a lower IQ and more non-sexual crimes than +CSO-P; and, on average, the highest PCL-R scores in the sample. 49% of +CSO-P and 19% of +CSO-P were predominantly homosexually oriented (*χ*² = 7.28, *P* = 0.0263) (this information was missing for 1 +CSO-P, 3 +CSO-P, and all NSOs), and median scores on the SSPI were the maximum of 5 for +CSO-P (min = 3, max = 5) and 3 for +CSO-P (min = 2, max = 5) (*χ*² = 7.48, *P* = 0.0293). Among +CSO-P, pedophilia diagnoses were marked as ‘exclusive’ for 17 (77.3%) subjects and as ‘non-exclusive’ for 2 (9.1%) (information was missing for the remaining 3 subjects). Among +CSO-P, 10 subjects (47.6%) had victims above 16; 5 of those had a pedophilia diagnosis (23.8% of all +CSO-P) in their file. Note, that one additional subject who had a pedophilia diagnosis and no convictions for sexual assault against an adult was sorted into the +CSO-P group due to a) his generally deviant behavior as expressed by a high number of (violent) crimes, b) the violence of the CSO, and c) allegations of rape by other inmates against him. Groups did not differ with regard to total brain volume, overall gray matter, white matter, or cerebrospinal fluid volume. In addition to the instances of missing information named above, information was missing in three NSOs for axis I diagnoses, in two for alcohol and substance use, and in all for paraphilia diagnoses.

Overall, no subject met criteria for any axis I disorder except for one NSO, who had been diagnosed with posttraumatic stress and anxiety. Substance use diagnoses, if present, referred to Cannabis use in all groups and to Cocaine and polydrug use in some +CSO-P. If subjects met criteria for any personality disorder, it was of antisocial personality disorder (see Table 1).

**SBM component loadings**

A MANOVA on gray matter volume data with group as the sole factor produced a significant result (*F*(*N*-group) = 1.8593, *F*(2, 60) = 1.983, *P* = 0.0299), which was confirmed by a rank-based MANOVA (Bartlett’s *χ*(62) = 3282.7, *P* < 0.001). A subsequent series of 30 one-way ANOVAs with only group as predictor, revealed a significant difference between groups in component 22 (*F*(22, *F*(2, 60) = 8.875, *P* = 0.0126), which stayed significant with the introduction of age (*F*(1, 49) = 3.872, *P* = 0.0548), IQ (*F*(1, 49) = 0.106, *P* = 0.747), handedness (*F*(2, 49) = 2.352, *P* = 0.106), medication (*F*(1, 49) = 4.166, *P* = 0.0467), substance use (*F*(2, 49) = 1.635, *P* = 0.2054), and alcohol use (*F*(2, 49) = 0.958, *P* = 0.3906; *F*group(2, 49) = 11.374, *P* < 0.001; *F*model(11, 49) = 3.707, *P* < 0.001, *R*2adj = 0.332) (see Fig. 1). Note, that *F*group increased with the introduction of the covariates, possibly indicating moderation effects with the covariates. Among the covariates, age produced a borderline significant and medication a significant effect. Step-wise model comparisons revealed the best model to be one including group (*F*(2, 54) = 11.313, *P* < 0.001), age (*F*(1, 54) = 3.851, *P* = 0.0549), handedness (*F*(2, 54) = 2.339, *P* = 0.1061), and medication (*F*(1, 54) = 4.144, *P* = 0.0467) as...
| Table 1. Demographic, psychological, criminological, and morphological information on all subjects |
|-----------------------------------------------|
| +CSO+P | +CSO-P | NSO |
| CT/n   | (Var/%) | CT/n   | (Var/%) | CT/n   | (Var/%) | Test statistic | Pairwise group comparisons |
| N      |         |        |         |        |        |               |                           |
| 22     | 21      | 20     |         |        |        |               |                           |

Demographic and physical information

| Age     | 44.86 (9.26) | 44.24 (9.90) | 36.30 (5.35) | F = 6.52** | +CSO+P > NSO |
| Years of school | 11 (8–12) | 12 (9–12) | 11.5 (7–12) | H = 1.13 |
| College education | 9 (41%) | 3 (14%) | 7 (35%) | χ² = 3.94 |
| Handedness |            |            |            |            |
| Both     | 3 (14%) | 3 (14%) | 1 (5%) | χ² = 1.61 |
| Right    | 17 (77%) | 17 (81%) | 18 (90%) |            |
| Left     | 2 (9%) | 1 (5%) | 1 (5%) |            |

Psychological and psychiatric information

| IQ (WAIS-III) | 102.32 (12.01) | 93.14 (9.23) | 100.80 (15.81) | F = 3.24* | +CSO+P > +CSO-P |
| PCL-R       | 17.87 (5.61) | 23.70 (6.12) | 18.91 (8.05) | F = 4.65* | +CSO+P < +CSO-P |

DSM-IV diagnoses

|                       |     |     |     |            |                           |
|-----------------------|-----|-----|-----|------------|----------------------------|
| Axis I                |     |     |     |            | +CSO+P > NSO               |
| Alcohol use           |     |     |     |            | +CSO+P > NSO               |
| Abuse                 | 3   | 6   | 6   | 30%        | +CSO+P > +CSO-P            |
| Depend                | 1   |     |     |            | +CSO+P > +CSO-P            |
| Substance use         |     |     |     |            | +CSO+P > +CSO-P            |
| Abuse                 | 1   | 6   | 2   | 10%        | +CSO+P > +CSO-P            |
| Depend                | 3   | 1   | 1   | 5%         | +CSO+P > +CSO-P            |
| Axis II               | 7   | 11  | 3   | 15%        | +CSO+P > +CSO-P            |

Paraphilias

|                      |     |     |     |            |                           |
|----------------------|-----|-----|-----|------------|----------------------------|
| Exhibitionism        |     | 1   |     | 5%         | +CSO+P > +CSO-P            |
| Sadism               | 2   |     |     | 10%        | +CSO+P > +CSO-P            |
| NOS                  | 3   | 11  | 3   | 52%        | +CSO+P > +CSO-P            |

Criminological information

|                     |     |     |     |            |                           |
|---------------------|-----|-----|-----|------------|----------------------------|
| Total crimes        | 14.5 (4–48) | 18.5 (6–71) | 10 (2–32) | H = 6.41* | +CSO+P > NSO               |
| Non-violent crimes  | 8   (0–36) | 11 (1–50) | 5 (0–26) | H = 6.86* | +CSO+P > NSO               |
| Violent crimes      | 8   (2–22) | 9 (4–32) | 2 (1–6) | H = 32.67† | +CSO+P > +CSO-P            |
| Non-sexual          | 0   (0–10) | 3 (0–11) | 2 (1–6) | H = 8.82* | +CSO+P > +CSO-P            |
| Sexual              | 5.5  (2–14) | 5 (3–31) |     |            | W = 280.00                 |
| Adult victims       | 0    (0) | 1 (0–26) |     |            | W = 125.50**               |
| Child victims       | 3    (1–12) | 2 (1–7) |     |            | W = 330.00*                |
| Male                | 2    (0–7) | 0 (0–2) |     |            | W = 341.50**               |
| Extrafamilial       | 2    (0–11) | 2 (0–6) |     |            | W = 241.00                 |

Morphological information and medication

|                     |     |     |     |            |                           |
|---------------------|-----|-----|-----|------------|----------------------------|
| TBV                 | 1414.33 (153.01) | 1484.07 (118.49) | 1486.72 (126.90) | F = 2.01 |
| GM                  | 660.13 (77.16) | 673.26 (91.30) | 686.05 (50.83) | F = 0.62 |
| WM                  | 466.59 (69.38) | 489.22 (54.82) | 500.06 (46.47) | F = 1.84 |
| CSF                 | 287.61 (76.49) | 321.59 (155.44) | 300.61 (107.25) | H = 0.07 |
| Medication          | 7    (32%) | 7 (33%) |     |            | χ² = 8.39                  |

*P < 0.05.
**P < 0.01.
†P < 0.001; CT = central tendency, means for normally distributed numeric variables, medians for non-normally distributed variables, n for count data; Var = variability, standard deviations for normally distributed numeric variables, min-max ranges for non-normally distributed variables, percentages for count data; Adult victims = 17 years of age and older; Child victims = 0–10 years of age.
‡Axis I diagnoses refer to time of assessment, alcohol and substance use information refer to lifetime use.
§Crimes comprise all crimes, including those admitted to but not necessarily prosecuted for. Percentages are indicated as proportion of total n in group, regardless of missing data.
Graphical display of gray matter clusters in SBM (source-based morphometry) component C22, exhibiting a statistically significant difference between groups. Axial view slice montage, height threshold $T > 2.00$, no extend setting, displaying positive contrast $t$-values, produced in bspmview (https://github.com/spunt/bspmview) in MATLAB. Slices are chosen automatically by bspmview based on maxima localizations.

Fig1

Average gray matter in component clusters

Table 2 lists all neuroanatomic structures indicated in the 15 clusters of C22 that exceeded 300 voxels ($T > 2.00$).

Two cerebellar clusters (7705 and 911 vox) were located in the anterior (lobules IV and V) and posterior (lobules VIIA, Crus I and II, and VIIIA) vermis, respectively, with the first cluster paravermally also reaching into the right posterior cerebellum, and the second one reaching into the left occipital cortex. Two further cerebellar clusters (1907 vox in lobules VI, VIIA, Crus I, and VIIIB, and 739 vox in lobules VIIIA/B, IX, and X) were posteriorly and laterally situated, with the right cluster reaching into the right inferior temporal and fusiform gyri. Four clusters (3066, 2001, 587, and 403 vox) were situated in the frontal lobe, comprising the bilateral precentral gyri (premotor area), dorsomedial/dorsolateral prefrontal cortex (DM/DLPFC), inferior frontal junction (IFJ), and the left medial OFC (mOFC) reaching into the right mOFC, including voxels in the frontal pole. In the parietal lobe, in addition to two clusters (401 and 1111 vox) in the bilateral medial prefrontal cortex (MPC), a right-hemispheric cluster (393 vox) was located in the superior parietal lobule, while a left cluster (354 vox) lay in the inferior parietal lobule, more specifically the intraparietal sulcus. Finally, one cluster each in the left (665 vox) and right (325 vox) basal ganglia emerged, comprising the bilateral ventromedial putamen and left ventral caudate. Overall, the right hemisphere was slightly more impacted than the left.

Unsurprisingly, a MANOVA of the 10 mm spheres surrounding the 37 peak voxels in the 15 biggest clusters (>300 vox) with group as the sole predictor again yielded a significant result ($\Lambda_{Roy} = 4.14, F(2, 60) = 2.612, P = 0.0076$). However, none of the 37 one-way ANOVAs (with group as the only predictor) computed as a follow-up remained significant after correcting for multiple comparisons.

An examination of smaller clusters using the SPM Anatomy Toolbox (<300 vox, $T > 2.00$; see Table 3) and the Brainnetome Atlas (<300 vox, no height threshold; see Table S2 for assignments) revealed abnormalities mirroring the structures in the bigger clusters in the respective opposite hemisphere (right inferior and left superior parietal lobule, left inferior temporal and fusiform gyri, right occipital lobe, right ventral caudate). Additionally, they included the bilateral postcentral gyri, the right temporal pole, the right superior and middle temporal gyri, the bilateral posterior parahippocampal gyrus, medial cingulate, and hippocampus, and revealed that the basal ganglia clusters spread into the left dorsal caudate and bilaterally into the dorsolateral putamen, nucleus accumbens, and globus pallidus.

Anatomically defined ROIs

A MANOVA for average gray matter volume in the 21 anatomically defined ROIs also yielded a significant result for group ($\Lambda_{Roy} = 1.078, F(2, 60) = 2.1, P = 0.0205$). None of the results for the 21 follow-up one-way ANOVAs (group as only predictor) survived correction, however.
### Table 2. Clusters bigger than 300 vx and above threshold of $T = 2$ encompassed in C22 showing significant gray matter volume reduction in CSO groups relative to the NSO group

| Lobe/Structure | Cluster size | Hem | Maximum localization | Prob | BA |
|----------------|--------------|-----|----------------------|------|----|
| Cerebellum‡  | 7705         | B   | −50 −6               | 8.18 | R  |
| VI, VIIA Crus I (Hem), VIIIB | 1907§  | R   | −42 −50              | 3.39 | R  |
| VIIA Crus I (Hem), Crus II (Hem/Verm), VIIIA (Verm) | 911  | B   | −83 −33              | 3.44 | R  |
| VIIIA, VIIIB, IX, X (Hem) | 739  | L   | −27 −39 −48          | 3.70 | L  |
| Frontal lobe | 3066         | R   | 30 −6 50              | 5.80 | R  |
| Middle frontal gyrus | 2001  | L   | −14 38 4.12          | L    | 8  |
| Middle frontal gyrus | 36      | 9   | 38 5.08              | R    | MFG IFJ 8 |
| Middle frontal gyrus | 33      | 17  | 59 5.01              | R    | MFG A6vl 8 |
| Parietal lobe | 403          | R   | 41 41 2.96           | R    | MFG A8vl 9 |
| Superior parietal lobule | 393  | R   | 14 −69 56            | 2.81 | R    |
| Inferior parietal lobule | 354  | L   | −32 −56 41           | 3.22 | L  |
| Occipital lobe | 1111  | L   | −15 −62 26           | 6.00 | L  |
| Middle occipital gyrus | 430  | R   | 33 −81 23            | 2.97 | R  |
| Temporal lobe | 1907§  | R   | −47 −29 4.01         | R    | Area FG 4 77% |
| Basal ganglia | 665          | L   | −20 15 −3            | 3.23 | L  |
| Caudate nucleus | 325   | R   | 21 15 −2             | 3.11 | L  |

†As assigned by SPM Anatomy Toolbox.
‡Cerebellum nomenclature of Schmahmann et al., lobules if not otherwise indicated.
§Same cluster.
¶Area in occipital lobe.

General localization of clusters and maxima was identified using the Anatomy Toolbox implemented in SPM. Structure assignment was also done using the SPM Anatomy Toolbox and complemented by assignment via the Brainnetome Atlas; in general, assignment via the two tools did not conflict. Where no probabilistic assignment was possible via the Anatomy Toolbox, only Brainnetome assignments are given (as indicated by the absence of a probability estimate for the assignment). A full table of Brainnetome abbreviations is available in the Supplement (Table S1) and via http://atlas.brainnetome.org/download.html. Brodmann Areas were assigned using the SPM Anatomy Toolbox or, when unavailable there, using the BioImage Suite Web 1.0.0 MN12TAL online client (https://bioimagesuiteweb.github.io/webapp/). Coordinates of local maxima are given in MNI space (Montreal Neurological Institute, www.bic.mni.mcgill.ca).

L = left; R = right; B = both; BA = Brodmann Area; Hem = hemisphere; Lob = lobule; Prob = probability of assignment; Verm = vermis.
Table 3. Clusters smaller than 300 vx and above threshold of $T = 2$ encompassed in C22 showing significant gray matter volume reduction in CSO groups relative to the NSO group

| Lobe/Structure | Cluster Size | Hem | x  | y  | z  | T  | Prob | BA |
|---------------|-------------|-----|----|----|----|----|------|----|
| Cerebellum    |             |     |    |    |    |    |      |    |
| VIIa Crus I (Hem) | 40   | L   | −44| −42| −39| 2.31| L    | 74% |
| VIIa Crus I (Hem), Crus II (Hem) | 18   | R   | 41 | −73| −45| 2.22| R    | 60% |
| Frontal lobe |             |     |    |    |    |    |      |    |
| Orbitofrontal cortex | 234  | B   | 8  | 15 | −24| 2.73| R    | 97% 11 |
| Superior medial gyrus | 189  | R   | 9  | 27 | 61 | 2.86| R    | 6 |
| Orbitofrontal cortex | 157  | L   | −29| 33 | −12| 2.80| L    | 37% 47 |
| Middle frontal gyrus | 77   | R   | 26 | 51 | 1  | 2.88| R    | 74% 10 |
| Superior frontal gyrus | 73   | L   | −20| 35 | 34 | 2.72| L    | 9 |
| Middle frontal gyrus | 51   | L   | −35| 57 | 13 | 2.55| L    | 10 |
| Posterior-medial frontal cortex | 49    | L   | −9 | −16| 48 | 2.63| L    | 6 |
| Precentral gyrus | 26   | L   | −42| −1 | 36 | 2.22| L    | 6 |
| Inferior frontal gyrus | 9    | L   | −38| 36 | 10 | 2.20| L    | 46 |
| Posterior-medial frontal cortex | 5    | L   | −5 | −12| 75 | 2.12| L    | 6 |
| Parietal lobe |             |     |    |    |    |    |      |    |
| Postcentral gyrus | 231  | L   | −39| −37| 63 | 2.72| L    | 43% 1 |
| Postcentral gyrus | 78   | R   | 42 | −39| 60 | 2.51| R    | 40% 1 |
| Paracentral lobule | 55   | R   | 9  | −37| 51 | 2.32| R    | 40% 5 |
| Precuneus | 20   | R   | 12 | −57| 67 | 2.28| R    | 59% 7 |
| Occipital (Extra) Striate cortex | 121  | B   | 0  | −84| −5 | 2.37| L    | 63% 18 |
| (Extra) Striate cortex | 119  | R   | 20 | −66| 7  | 3.00| R    | 66% 17 |
| Middle occipital gyrus | 32   | L   | −33| −81| 6  | 2.33| L    | 60% 18 |
| Superior occipital gyrus | 25   | L   | −20| −81| 27| 2.37| L    | 19% 19 |
| Cuneus | 13   | R   | 12 | −90| 27 | 2.08| R    | 57% 19 |
| Temporal Inferior temporal gyrus | 142  | L   | −50| −37| −18| 3.20| L    | 36% 20 |
| Temporal pole area | 141  | R   | 48 | 17 | −24| 2.27| R    | 38 |
| Middle temporal gyrus | 121  | R   | 45 | −63| 6  | 2.88| R    | 9% 38 |
| Fusiform gyrus | 107  | R   | 36 | −10| −29| 3.08| R    | 5% 19 |
| Heschls gyrus | 97   | R   | 51 | −10| 9  | 2.26| R    | 31% 1 |

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robust network of reduced gray matter volume in CSOs relative to per se by pedophilia which may indicate that a remainder of variance may be explained (despite a trend placing + in the Supplement (Tables S3 to S24).

The present study is the first to present a structural MRI comparison of +CSO+P, +CSO-P and NSOs. Using a multivariate whole-brain analysis approach, we identified a widespread, interrelated, and robust network of reduced gray matter volume in CSOs relative to NSOs, but no significant difference between +CSO+P and +CSO-P (despite a trend placing +CSO-P between +CSO+P and NSOs, which may indicate that a remainder of variance may be explained by pedophilia per se, though this is slightly at odds with other current works in the field\cite{35}). This network encompassed the bilateral frontal (premotor area, DM/DLPFC, mOFC/fronatal pole, inferior frontal junction), parietal (postcentral gyrus, medial precuneus, inferior and superior parietal lobule), temporal (inferior temporal, fusiform, and parahippocampal gyri, right middle and superior temporal gyrus and temporal pole), and occipital lobe. In addition, it included clusters in the bilateral basal ganglia (ventromedial and dorsolateral putamen, ventral caudate, nucleus accumbens, globus pallidus, left dorsal caudate), the bilateral cerebellum (bilateral [para-] vermal lobules IV, V, VII [Crus I and II], and VIII, as well as right lateral lobules VI-VIII and left lateral lobules VIII-X), and the bilateral medial cingulate and hippocampus. Abnormalities were more pronounced in the right hemisphere. No structure drove this multivariate finding particularly.

The network character of our findings was additionally underlined by two aspects. First, our findings encompassed important associative structures, including the precuneus and the DLPFC, the basal ganglia, and the cerebellum. The basal ganglia and cerebellum especially have been found to form (complementary) parallel closed loops with cortical structures,\cite{44} mediating the integration of various cognitive and emotional processes and contributing to several higher-level functions including social cognition.\cite{65,66} Interestingly, loci with abnormal gray in CSOs in our results seemed to more strongly attributable to cognitive than emotional processes in both circuit bases.\cite{67} Second, our non-cerebellar clusters appeared to exhibit connectivity with each other as informally identified using the Brainnetome Atlas. Overall, this may indicate connectivity-related neural impairments in CSOs, affecting higher-level cognitive and inhibitory functioning, in line with neuropsychological findings.\cite{68}

Though no study thus far has conducted the same group comparison as we did, our results show overlap with the (sometimes uncorrected) findings of studies comparing +CSO+P to non-offending controls\cite{28,32} (see the Supplement for regions). They also overlap with results of reduced gray in +CSO+P compared to -CSO+P specifically.\cite{40,45} We are furthermore not the first to identify network-related impairments of brain structure (and function)\cite{24,25} in CSOs. In fact, Cantor et al.,\cite{34} argued that connectivity-based abnormalities are the only findings on brain structure in +CSO+P not attributable to low statistical power,\cite{32} as they identified no abnormal gray but abnormal white matter in CSOs compared to NSOs\cite{34} and healthy controls.\cite{35} Of note, the gray matter structures connected by their white matter findings overlap with the loci we identified (left DLPFC, frontal pole, superior parietal lobule, occipital cortex). Furthermore,

### Table 3. (Continued)

| Lobe/Structure \^ | Cluster Size | Hem | MNI coordinates | Maximum localization | Prob\(^\dagger\) | BA |
|------------------|-------------|-----|-----------------|-----------------------|----------------|----|
|                  |             |     |                 |                       |                |    |
| Frontal          |             |     |                 |                       |                |    |
| Middle temporal  | 24          | L   | −39 −64 12     | 2.37 L               | OeG_L_4.2      | 19 |
| Fusiform gyrus   | 23          | L   | −32 −61 −14    | 2.36 L               | Area FG1       | 37 |
| Superior temporal| 19          | R   | 59 −3 −3       | 2.12 R               | Area TE 1.2    | 22 |
| Middle temporal  | 10          | R   | 54 −13 −18     | 2.13 R               | FuG_L_3.3      | 21 |
| Fusiform gyrus   | 9           | L   | −35 −16 −26    | 2.09 L               | FuG_L_3.1      | 36 |
| Fusiform gyrus   | 2           | R   | 48 −69 −17     | 2.01 R               | Area hOe44a    | 53 |
| Subcortical      |             |     |                 |                       |                |    |
| Midcingulate     | 64          | R   | 2 −13 36       | 2.17 R               | CG_R_7.6       | 24 |
| Midcingulate     | 24          | R   | 11 −15 48      | 2.40 R               | PCL_R_2.2      | 24 |
| Midcingulate     | 18          | L   | −11 9          | 2.21 L               |                |    |

\^As assigned by SPM Anatomy Toolbox.
\^Cerebellum nomenclature of Schmahmann et al.,\cite{63} lobules if not otherwise indicated.

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Correlational analyses

In contrast to former findings, no significant correlation of SSPI, PCL-R scores, or number of violent crimes with gray matter volume was identified in our data, neither when examining the decomposed C22 clusters, nor when examining the anatomically defined ROIs. This was the case both for all CSOs and for each CSO group on its own. Correlation values and pertaining significance tests can be found in the Supplement (Tables S3 to S24).

Discussion

The present study is the first to present a structural MRI comparison of +CSO+P, +CSO-P and NSOs. Using a multivariate whole-brain analysis approach, we identified a widespread, interrelated, and robust network of reduced gray matter volume in CSOs relative to NSOs, but no significant difference between +CSO+P and +CSO-P (despite a trend placing +CSO-P between +CSO+P and NSOs, which may indicate that a remainder of variance may be explained by pedophilia per se, though this is slightly at odds with other current works in the field\cite{35}). This network encompassed the bilateral frontal (premotor area, DM/DLPFC, mOFC/fronatal pole, inferior frontal junction), parietal (postcentral gyrus, medial precuneus, inferior and superior parietal lobule), temporal (inferior temporal, fusiform, and parahippocampal gyri, right middle and superior temporal gyrus and temporal pole), and occipital lobe. In addition, it included clusters in the bilateral basal ganglia (ventromedial and dorsolateral putamen, ventral caudate, nucleus accumbens, globus pallidus, left dorsal caudate), the bilateral cerebellum (bilateral [para-] vermal lobules IV, V, VII [Crus I and II], and VIII, as well as right lateral lobules VI-VIII and left lateral lobules VIII-X), and the bilateral medial cingulate and hippocampus. Abnormalities were more pronounced in the right hemisphere. No structure drove this multivariate finding particularly.

The network character of our findings was additionally underlined by two aspects. First, our findings encompassed important associative structures, including the precuneus and the DLPFC, the basal ganglia, and the cerebellum. The basal ganglia and cerebellum especially have been found to form (complementary) parallel closed loops with cortical structures,\cite{44} mediating the integration of various cognitive and emotional processes and contributing to several higher-level functions including social cognition.\cite{65,66} Interestingly, loci with abnormal gray in CSOs in our results seemed to more strongly attributable to cognitive than emotional processes in both circuit bases.\cite{67} Second, our non-cerebellar clusters appeared to exhibit connectivity with each other as informally identified using the Brainnetome Atlas. Overall, this may indicate connectivity-related neural impairments in CSOs, affecting higher-level cognitive and inhibitory functioning, in line with neuropsychological findings.\cite{68}

Though no study thus far has conducted the same group comparison as we did, our results show overlap with the (sometimes uncorrected) findings of studies comparing +CSO+P to non-offending controls\cite{28,32} (see the Supplement for regions). They also overlap with results of reduced gray in +CSO+P compared to -CSO+P specifically.\cite{40,45} We are furthermore not the first to identify network-related impairments of brain structure (and function)\cite{24,25} in CSOs. In fact, Cantor et al.,\cite{34} argued that connectivity-based abnormalities are the only findings on brain structure in +CSO+P not attributable to low statistical power,\cite{32} as they identified no abnormal gray but abnormal white matter in CSOs compared to NSOs\cite{34} and healthy controls.\cite{35} Of note, the gray matter structures connected by their white matter findings overlap with the loci we identified (left DLPFC, frontal pole, superior parietal lobule, occipital cortex). Furthermore,
in a review examining functional connectivity between gray matter regions previously identified as abnormal in +CSO+P and key areas of sexual processing, Poeppl et al., suggested that altered brain structure in these men may affect neural networks for sexual processing through disrupted functional connectivity. In parallel to this interpretation, our findings overlap with the inhibitory (mOFc, caudate), cognitive (appraisal: inferior temporal cortex; attention: superior and inferior parietal lobe), and autonomic/endocrine (putamen) components of the neurophenomenological model of sexual arousal in men. This network has been found to be activated similarly in pedophiles and teleiophiles when each group is confronted with their preferred stimuli, but has thus far not been explicitly studied in sex offenders vs. non-sexual-offenders.

Our results suggest that structural brain abnormalities may be pertaining to CSO rather than to pedophilia, a conclusion also drawn in former studies comparing +CSO+P and -CSO+P. Using a multivariate, whole-brain analysis approach, we were able to present an unbiased comparison with a minimal loss of statistical power. Our results therefore are a rather strong testament to the presence of brain abnormalities in pedophilic men. Apart from group, no variable in our data showed significant covariance with gray matter, and the group variable remained significant after the introduction of covariates. This included number of violent crimes and psychopathy scores, pointing toward the interpretation that a general proneness to violence may not be explanatory for the abnormalities at hand. However, CSOs had committed significantly more violent crimes and were older than NSOs, possibly reflecting that the NSOs in our sample were incarcerated earlier, providing less time to further commit violent acts. Though age did covary slightly with C22 based on its non- but marginally significant result in the model, its predictive power was neither responsible for nor greater than that of group.

Our study exhibits several limitations. First, though we maximized statistical power when answering our main research question, our sample size was limited. Our findings therefore need to be considered preliminary and should be confirmed by larger scale studies. Second, allocation to groups on the basis of criminological data was not ideal and led to some subjects with a DSM-IV pedophilia diagnosis being sorted into the non-pedophilic group. Identifying pedophilic interest (among CSOs) is a notorious issue, and though criminal records can give an indication, a multimodal diagnostic process would be superior. Given that the identification of covarying loci in SPM was blind to group allocation however, this did not impact the identification of the later significant gray matter loci, thereby decreasing the influence of possible misallocations. Third, we did not include -CSO+P subjects, a group needed to fully disentangle P and CSO. This addition should therefore be addressed in future research, despite the well-known difficulties of assembling samples of larger sizes in the field, which also challenged the attainment of the present sample. Finally, though our main result points to network-related abnormalities, we did not follow-up with a formal connectivity analysis of our findings.

Overall, our results are a testament to, possibly network-related, neural impairments in CSOs. These abnormalities are unlikely correlates of general violence but may be pertaining to sexual violence (against children). Future research should seek to provide well-powered P/CSO-x2 designs and explore multi-instead of univariate analysis approaches further.

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Disclosure statement
The authors declare no conflict of interest.

Author contributions
Conception and design of study: M.K., K.J., K.K., C.H. and J.M. Acquisition and analysis of data: M.K., P.N. and C.H. Drafting the manuscript or figures: M.K.

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Supporting information
Additional Supporting Information may be found in the online version of this article at the publisher’s web-site:

Appendix S1: Supplementary Information