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Original Article

Neuroimaging in sexual offenses and paraphilia: A call to harmonize current clinical and imaging assessments in sexual offenses and paraphilia

Naghmeh Mokhber[1]; David Streiner[2]; Sébastien Prat[3]; Niloofar Nikjoo[4]; *Gary Chaimowitz[3]

[1]*Department of Psychiatry and Behavioural Neurosciences, University of Western Ontario, London, ON, Canada. Psychiatry and Behavioral Sciences Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.*
[2]*Department of Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton, ON, Canada. Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, ON, Canada.*
[3]*Department of Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton, ON, Canada.*
[4]*Department of Psychiatry and Behavioural Neurosciences, University of Western Ontario, London, ON, Canada.*

Abstract

Introduction: The advent of brain imaging studies has provided a chance to assess behavioral changes in patients with psychiatric disorders and compare the results with healthy individuals. These studies have clinical and research implications especially for forensic clinicians, and psychologists who not only diagnose psychiatric disorders but also need to determine the level of criminal responsibility and assess the level of risk that patients may pose for the safety of the public. However, few studies have reviewed the current literature systematically. The aim of this article is to summarize and categorize available studies.

Materials and Methods: We performed a comprehensive search to identify all available articles on neuroimaging findings of paraphilia.

Results: Sixty hundred and fifty five papers were reviewed for this study, out of which 56 articles were selected. Papers were classified according to sexual disorder types and were categorized into case reports and case series (n= 25), and case-control studies (n= 31). Important findings of the selected papers were summarized and areas of the brain involvement were highlighted.

Conclusion: Structural and functional neuroimaging may elucidate the neuroanatomical network of paraphilia. These findings have research and clinical implications in the field of forensic psychiatry.

Keywords: Masochism, Neuroimaging, Paraphilia, Pedophilia, Sadism.

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***Corresponding Author:**
Department of Psychiatry and Behavioural Neurosciences, University of Western Ontario, London, ON, Canada.
chaimow@mcmaster.ca
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Introduction

The advent of structural and functional neuroimaging has provided a great opportunity to study normal physiology and pathophysiology of neurobehavioral changes, such as changes in sexual activity (1). Logically, sexual arousal may originate through central processes (2) via different neural pathways (3).

Although it was first believed that limited parts of the brain, such as the orbitofrontal cortex, claustrum, anterior cingulate cortex, caudate, putamen, and the hypothalamus are responsible for sexual arousal (4,5), it was later shown that psychological and physiological aspects of sexual arousal need activation from a significant widespread network of neurons in a neurophenomenological model (6).

While putamen and claustrum are often activated during sexual arousal, the temporal and parietal cortices are deactivated (7). The temporal and parietal cortices also have a significant impact on the cognitive and motivational excitatory components of sexual arousal (6).

Patients with a range of brain lesions may present or develop sexual disorders needing further forensic assessments. These are often very challenging cases, and it can be difficult even for forensic psychiatrists to determine their level of criminal responsibility. Despite the devastating psychosocial effects of sexual offenses on victims and societies, relevant neurobiological studies on sexual offenders are still scant, and their results vary significantly due to extremely different methodological designs (Tables 1-4).

This article provides an overview of the structural and functional neuroimaging findings of sexual offenders and patients with paraphilia.

Materials and Methods

Using PubMed (1946 to November 2019), Scopus (1966 to November 2019), EMBASE (1947 to November 2019), Web of Science (1900 to November 2019), PsycINFO (1967 to November 2019), and the Cochrane Database of Systematic Reviews, a comprehensive literature search was performed in order to identify all available articles on neuroimaging findings of sexual offenders. There were no language or publication restrictions for the studies' inclusion. Keywords included paraphilia, pedophilia, sadism, masochism, sadomasochism, frotteurism, voyeurism, exhibitionism, fetishism, sexual deviation, sexual offenses, sexual abuse, sexual harassment, sexual offender, sexual abuse, rape, sexual crime, criminals, and magnetic resonance imaging, magnetic resonance spectroscopy, functional neuroimaging, functional magnetic resonance imaging, tomography x-ray computed, nuclear medicine, single-photon emission computed tomography, and positron-emission tomography. In addition, a hand search was performed based on the references that were cited in previous review articles and meta-analyses. After deleting duplicates, we imported all references into the Covidence platform. Two independent authors reviewed all studies, starting with the title and abstract screening.

After a full-text review, studies reporting any sexual offense in subjects with or without paraphilia, reviewing paraphilia in those with or without a history of sexual crimes, were selected for this review. Other inclusion criteria include full-length reports; subjects with paraphilia underwent neuroimaging evaluations. An independent senior psychiatrist resolved any disagreement regarding the selection of studies. Selected studies were classified into two major groups: case reports/series and case-control studies.

Results

After a comprehensive search and review (Fig. 1), 56 articles were found, including 25 case reports and case series and 31 case-control studies.

Important information regarding subjects' clinical manifestations of paraphilia, methods of evaluation, diagnostic criteria, the localization of a lesion, and associated neuropsychiatric symptoms were extracted. Table 1 summarizes case reports in sexual offenders and paraphilia, assessing a range of neuroimaging structural and functional techniques. Studies using structural (i.e., brain Computerized Tomography (CT) and Magnetic Resonance Imaging (MRI)) and functional imaging (i.e., functional MRI, Positron Emission Tomography (PET) with a case-control design are summarized in Table 2 (n= 11) and Table 3 (n= 16). Data regarding serial killers and patients with sadism were limited to a few studies (Table 4).

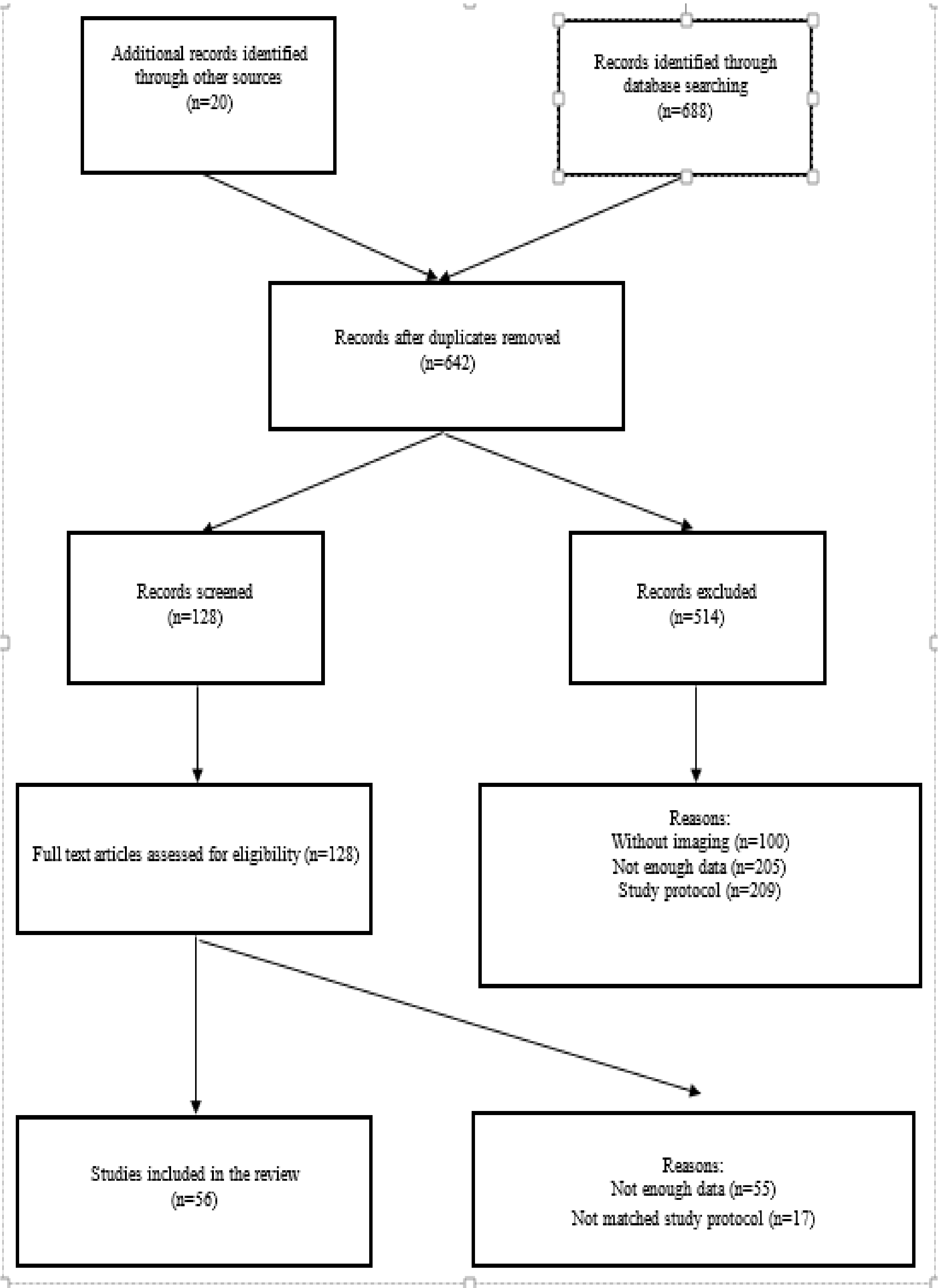

Figure 1. Neuroimaging in paraphilia: Systematic Flowchart

Table 1. Neuroimaging in paraphilia: A summary of case reports with anatomical localization

Studies/ authors	Sexual history and diagnosis/Neuropsychiatric symptoms	Lesion/findings	Evaluation
(Hooshmand and Brawley, 1969)	2 cases with exhibitionism.	Temporal lobe seizures: Abnormal calcification in the sylvian region.	Skull X-ray and angiogram
(Lesniak et al., 1972)	A previously healthy man with a gradual development of a range of paraphilia, including harlotry, incestuous intercourse with his under-age daughter, sodomy, hetero/homosexual pedophilia, masochism with some symptoms of sadism, coprolalia, exhibitionism, pedophilia and exhibitionism. Neuropsychiatric Symptoms: decreased intelligence.	Brain tumour: benign glioma or meningioma in the basal paracentral part of the right forehead lobe.	Pneumoencephalography
(M. F. Mendez et al., 2000)	2 patients with late-life homosexual pedophilia. Both were professional men with recent increases in sexual behavior.	Frontotemporal dementia: hippocampal sclerosis, and prominent right temporal lobe hypometabolism in 18-fluorodeoxyglucose PET.	PET
(Dreßing et al., 2001)	A 33-year-old homosexual pedophilic sex offender; Two cases of teleiophilia attracted to women.	A significant activation of the right orbitofrontal cortex, left fusiform gyrus, visual cortex, brainstem, right anterior cingulate cortex. The left fusiform gyrus was stronger recruited during pictures of boys in bathing suits in pedophilic patient than during photographs of women in controls. Stronger recruitment of medial temporal and left frontal in controls but not in patients.	fMRI
(de Assis Aquino Gondim and Thomas, 2001)	A case of multiple sclerosis with episodes of greatly increased libido.	Frontal lobe dysfunction in imaging and neuropsychological studies.	MRI
(Frohman, Frohman, and Moreault, 2002)	Acquired sexual paraphilia in patient with multiple sclerosis with an obsessive and insatiable desire to touch women's breasts.	Multiple sclerosis: Active plaques in right sides of the hypothalamus and mesencephalon and extending into the right sides of the red nucleus, substantianigra, and internal capsule.	MRI
(Burns and Swerdlow, 2003)	Acquired pedophilia in a 40- year-old right-handed male with impulsive sexual behavior and pedophilia. Neuropsychiatric Symptoms: constructional apraxia, agraphia, suicidal ideation, headache, delayed recall, imbalance, and unconcerned about urinating on himself.	Brain tumor: Right obito frontal hemangiopericytoma.	MRI
(Nedopil et al., 2008)	A 47-year-old serial killer with sadism.	Gliotic scars in the frontal lobe and right hippocampus.	MRI
(Husted et al., 2008)	A late teenage male with history of kidnapping and rape of a young woman. Neuropsychiatric Symptoms: delay in developmental milestones (speech and language and low IQ), possible diagnoses of attention-deficit hyperactivity disorder with bad response to methylphenidate, oppositional defiant disorder, conduct disorder, various depressive mood disorders, and antisocial personality disorders; partial complex and absence seizures, treated with carbamazepine. Emotionally abused by alcoholic father, a history of closed head injury, cocaine, and alcohol abuse.	Atrophy of the left medial temporal lobe; more activation of frontal regions in ventromedial and ventrolateral for labeling than for matching and amygdala activation.	Structural and functional MRI
(Appelbaum, 2009)	A rapist.	Decreased function in the frontal lobe.	PET
(Gabison-Hermann, Pelletier, Taleb, and Bouleau, 2009)	A 37-year-old man, with temporal epilepsy, transient, atypical psychiatric states, including hypersexuality with qualitative changes in sex drive, obscene behavior, exhibitionism, masturbation and modified sexual orientation. Neuropsychiatric Symptoms: Blunted affect, inability to recognize significant people (visual agnosia).	Temporal lobe seizures: MRI was normal and interictal SPECT showed decreased cerebral perfusion in both temporal lobes	MRI/ SPECT
(Boris Schiffer, Gizewski, and Kruger, 2009)	A 38-year-old exclusive type (female children) pedophilic, treated with Leuopride acetate.	Reduced neuronal responsiveness to visual sexual stimuli	fMRI/ with visual sexual stimuli

(Bianchi-Demicheli, Rollini, Lovblad, and Ortigue, 2010)	Progressive sexual deviant behavior after a head trauma, the patient felt sexually aroused by seeing sleeping women as well as from taking care of their hands and nails while they were asleep. Neuropsychiatric Symptoms: dysexecutive syndrome, parietal-related bodily self-image disorder.	Fronto-parietal traumatic brain injury	MRI
(Müller, 2011)	A 16-year-old boy murderer with an autistic disorder and sadomasochism. Neuropsychiatric Symptoms: fearless, socially disruptive, impulsive- aggressive, as well as obsessive-compulsive, unable to learn from negative experiences, retarded in motor and mental development.	Hypointensities in amygdala-hippocampal complex bilaterally medial to both cornuainferiores corresponding to an amygdalo-hippocampalatrophy.	MRI
(Habermeyer et al., 2012)	A 43-year old male homosexual hedophilic, treated with Leuopride acetate.	A pretreatment activation of the right amygdala and adjacent parahippocampal gyrus decreased significantly with leuprolide acetate.	fMRI
(Moulier et al., 2011)	A 46-year-old pedophilic patient only attracted to boys, treated with Leuprolide acetate.	Pretreatment activations vanished in patients.	fMRI with visual sexual stimuli
(Othman et al., 2014)	A 65-year-old man with inappropriate sexual behavior and zoophilia.	Frontotemporal dementia	CT, brain MRI
(Masuda et al., 2014)	A 24-year-old male with fetishism since age 11.	Bilateral decrease in of CBF in temporal and occipital lobe	SPECT
(Kolta and Rossi, 2018)	18-year-old Caucasian male with a history of ASD, having suicidal thoughts after experiencing sexual fantasies; e.g. being aroused by anthropomorphic animal characters, violent sexual fantasy (sex with a girl and cut her head off).	Encephalomalacia on the axial section located in the right frontal lobe	CT without contrast
(Zheng, Lin, Ye, and Shi, 2017)	11-year-old boy (known case of X-linked adrenoleukodystrophy) with exhibitionism, progressive neurobehavioral symptoms, and reluctance to communicate and eat.	Altered signal intensities in bilateral frontal white matter, basal ganglia, and dorsal thalami, and a peripheral rim of contrast Enhancement.	MRI

Abbreviations (in alphabetical order): ASD: Autism spectrum disorder; fMRI: Functional Magnetic resonance imaging; MRI: Magnetic resonance imaging; PE:pneumoencephalography; PET: positron emission tomography; SPECT: single-photon emission computed tomography.

Table 2. Neuroimaging in paraphilia: A summary of case-control studies of pedophilia with structural imaging

Study/ Author	Population		Diagnoses	Setting		Age		Education		IQ		Evaluatio n	Results
	Case	Control		Case	Con trol	Case	Contr ol	Case	Contr ol	Case	Control		
(Hucker et al., 1986)	12 HS, 11 HOS, and 6 BS male pedophiles	12 non-violent non-sex offenders	SI	OC	OC	38.97± 13.91	25.39 ± 8.59 (Sig)	11.3± 3.07	12.15 ± 1.57	97.33	107.14 (Sig)	CT	Left temporo-parietal pathology in pedophilia.
(Langevin et al., 1989)	84 pedophilia	32 property offenders	Registered data base	-	-	-	-	-	-	HOS =93.9 1BS=1 04.88 HS=9.39	107.0 6 (Sig)	CT	No significant difference.
(Schiltz et al., 2007)	15 male pedophilia	NHC:15 matched	DSM-IV-R	HSF H	CO M	40± 8.9	37.3± 6.5	12.4± 1.5	14.3± 3.5	97± 14.5	110± 12	MRI	Subtle defects of the right amygdala in pedophilia.
(Boris Schiffer et al., 2007)	18 male non-exclusive Pedophila	NHC: 24 matched HS	DSM-IV	HSF H	CO M	37.67±7.9 9	33.63 ±7.07	10.8±1. 96	13.38 ±2.88(Sig)	101.8±8.21	110.1±8.5 1 (Sig)	MRI/1.5 T	Frontostriatal system and cerebellum involvement in pedophilia.
(Cantor et al., 2008)	65 Pedophilia	62 Non sexual Offender	SI	CAM H	FPO	36.4±1 3.5	36.9± 9. 4	12.2± 3	12.1 ±2.8	96.2 ±15.3	96.3 ±11.5	MRI/1.5 T	Significant negative associations between pedophilia and white matter volumes of bilateral Temporal and parietal lobes.

(Cantor & Blanchard, 2012)	19 Pedophilia, sexual orientation and exclusive type unknown	49 Hebephiles, and 47 Teleiophiles	SI	OC	OC	36.88± 11.82 (ALL)	36.88 ± 11.82 (ALL)	12.05±2.95	12.05 ± 2.95	NA	NA	MRI/1.5 T	More similar findings between hebephiles and pedophilia than that of teleiophilia.
(Poeppl et al., 2013)	9 pedophilia	11 Non sexual offenders	DSM-IV TR, ICD 10	HSFH	HSFH	45±8 (Sig)	29±6	NA	NA	92±18	100± 19	MRI/ 1.5T	Right amygdala,and gray matter decreased in the left dorsolateral prefrontal cortex and insular cortex in pedophilia.
(Gerwinn et al., 2015)	9 pedophilia, exclusive type, attracted to men	11 Non sexual offenders	DSM- IV TR	HSFH	HSFH	45±8 (Sig)	29± 6	NA	NA	92±18	100±19	T1-weighted and diffusion MRI / 3t	No significant difference between white matter and gray matter in pedophiles and teleiophiles.
(Fonteille et al., 2019)	15 male pedophilia	NHC: 15 matched HS, and HOS	DSM-IV-TR, ICD-10	OC	OC	42.0± 12.6	41.2± 16.2	16.6± 5.5	14.9± 4.1	≥70	≥70	MRI/ 1.5 T, and PET with VSS	The role of right inferior temporal gyrus in mediating sexual arousal of pedophilic cases.
(Lett et al., 2018)	73 male pedophilia with CSO, and 77 male pedophilia without CSO	133 teleiophiles	DSM-IV-TR/ ICD-10/ SI	COM	COM	39.8± 9.0 (P+CSO) and 34.2± 9.4 (P-CSO)	33.6± 10.2	NA	NA	NA	NA	MRI/ T1-weighted	Reduced cortical thickness-surface area, and white matter fractional anisotropy in child sexual offenders as compared to pedophilic without offense.
(B. Schiffer et al., 2017)	58 male pedophilia with CSO, and 60 male pedophilia without CSO	NHC: 101 male	DSM-IV-TR, ICD-10	COM	COM	40.1± 9.1 (P+CSO) and 34.4± 9.2 (P-CSO)	33.8± 10.5	NA	NA	39.8±9.8 (P+CSO) and 44.2±9.1 (P-CSO)	43.0±10.7	MRI/ T1-weighted	A significant association between a lower grey matter volume in the dorsomedial prefrontal or anterior cingulate cortex and a higher risk of re-offending in CSOs.

Abbreviations (in alphabetical order):
Age: years (Mean ± SD); ALL: All cases and controls; BS: Bisexual; CAMH: Centre for Addiction and Mental Health; COM: Community; CSO: Child Sexual Offence; CT: Computerized tomography; E:ducation: years (Mean ± SD); FPO: Federal probation offices; HOS: Homosexual; HS: Heterosexual; HSFH: high security forensic hospital; MRI: Magnetic resonance imaging; NHC: Normal healthy control; OC: Outpatient Clinic; SI: Structural Interview; Sig: Significant P value (<0.05); VSS: Visual Sexual Stimuli.

Table 3. Neuroimaging in paraphilia: A summary of case-control studies of pedophilia with functional imaging

Study/ Author	Population		Diagnosis	Setting		Age		Education		IQ		Evaluation	Results
	Case	Control		Case	Control	Case	Control	Case	Control	Case	Control		
(Cohen et al., 2002)	22 pedophilia, Non-exclusive, including one case with a history of child pornography	NHC:24	DSM-IV	CAP Behavior Associates	COM	38±8	37±10	11.77 ±3.1	14.54± 1.5(Sig)	7.59± 2.7(W R)	9.04± 2(WR)	PET	Neurodevelopmental abnormalities in the Temporal and frontal regions.
(Walter et al., 2007)	13 Pedophilia, sexual identity: not Known.	NHC 14 matched	DSM-IV	HSFH	COM	NA	NA	NA	NA	NA	NA	fMRI /1.5 T	Reduced activation in hypothalamus and lateral prefrontal cortex during visual erotic stimulation.

(Schiffer, Paul, et al., 2008)	8 Pedophilia, exclusive type attracted to women	NHC : 12 matched	DSM-IV	HSF H	CO M	36.1 ± 7.5	38.4 ± 9.4	11.15 ±1.73	12.81 ±2.46 (Sig)	52.14± 5.96	59.22 ± 9.86 (GW)	fMRI /1.5 T/ with VSS	Reduced activation of orbitofrontal cortex and dorsolateral of prefrontal cortex.
(Sartorius et al., 2008)	10 Pedophilia, unknown sexual orientation, attracted to boys	NHC:10 matched HS	ICD- 10	HSF H	COM	33.1 ± 8.9	35.3 ± 8.3	9 ± 0	9.2 ±0.4	91 ± 9	98 ±6	fMRI/ 1.5 T with VSS	Right amygdala activation in pedophilia.
(B. Schiffer et al., 2008)	11 Pedophilia, exclusive type attracted to male	NHC: 12	DSM-IV	HSF H	COM	37 ±7.5	32±6.8	11.15 ±1.73	12.81 ± 2.47(Sig)	52.56± 8.59(G W)	55 ±7.92	fMRI/ 1.5 T with VSS	A selectivity activation of the subcortical brain region related to reward, addictive and stimulus-controlled behavior.
(Poeppl et al., 2011)	9 Pedophilia, exclusive type, attracted to men	11 Non sexual offenders	DSM-IV TR	HSF H	HSFH	45± 8 (Sig)	29 ± 6	NA	NA	92±18	100±19	fMRI/ 1.5 T with VSS	Significant differences in cingulate gyrus and insular region.
(Ponseti et al., 2012)	24 including 11 HS and 13 HOS exclusive and non exclusive type Pedophilia	32 including 18 HS and 14 HOS teleiophilia	DSM-IV R	OC	COM	37± 5.9 HS, 33.5± 14.2 HOS	32.4± 8.2 HS 28.6± 5.7 HOS	NA	NA (higher)	11±3.1HS, 10.2±2.9HOS	11.8±2.3HS,11.8±2 HOS	fMRI/ 3T with VSS	Clinical applications of functional brain information to identify pedophiles.
(Benedikt Habermeyer et al., 2013)	8 HS exclusive pedophilia, including 5 cases only interested in pornography	NHC : 8 HS	DSM-IV TR	OC	COM	48.25± 9.15	46.25±8.38	NA	NA	116±12.12	124.88±13.91	fMRI/ 3T with VSS	Selective activation of the brain region related to reward and punishment in pedophilia.
(B. Habermeyer et al., 2013)	11 Pedophilia including 8 cases with HS and 3 HOS and 6 cases with children pornography	NHC:7 matched HS	DSM-IV TR	OC	COM	49±12.5	47±8.6	NA	NA	115.3± 20	118±6	fMRI/3T with Go/ No-GO task for response inhibition	The possible role of self- related processes in behavioral differences.
(Kärgel et al., 2015)	26 Pedophilia, including 8 HS and 18 HOS pedophilia	NHC : 14	DSM-IV TR	OC	COM	43.67±7.08 P+CSA, 28.07±5.71 P–CSA	32.86±9.89	NA	NA	37.75± 12.21 P+CSA, 45.69+/-9 P–CSA	37.38± 10.86 WAIS	fMRI/ 3T	Diminished functional activities in brain networks involved in motivational and socio-emotional process in pedophilia.

(Massau et al., 2017)	31 male pedophilia, including 10 HS and 21 HOS	NHC: 19, including 9 HS and 10 HOS	DSM-IV-TR	COM and FPO	COM	36.44± 8.01 (P+CSO) and 31.73± 6.49 (P-CSO)	33.47± 10.24	NA	NA	NA	NA	fMRI	An fMRI study showed the possibilities of different moral processing in pedophilic offenders as compared to healthy controls.
(Ristow et al., 2018)	10 male pedophilia	NHC: 10 matched	DSM-5	NA	NA	33.70 ±10.46	31.60 ±4.27	NA	NA	94.30 ±15.54	99.5 ±17.69	MRS	GABAergic deficits in the dorsal anterior cingulate cortex of pedophilic cases.
(Gibbels et al., 2019)	43 male convicted with CSO	31 male Non-convicted with CSO	DSM-IV/SI	FPO	COM	39.80 ± 9.0	40.4 ± 10.8	NA	NA	98.27 ± 18.95	100.26 ± 18.51	fMRI/3T with Go/ No-GO task for response inhibition	Similar clinical characteristics, neural activation, and behavioral inhibition performances among convicted and non-convicted pedophilic CSOs.
(Cazala et al., 2019)	25 male pedophilia	NHC: 24 male matched	DSM-IV-TR, ICD-10	OC	COM	42.2± 12.0	37.8± 12.8	16.0 ± 4.8	16.2± 3.2	≥70	≥70	fMRI/3T with VSS	In response to pictures of nude children, a random-effect statistical analysis showed a bilateral activation in the temporal cortices, the lateral occipital, and the declive of the cerebellar vermis in patients only.
(Kargel et al., 2017)	40 male pedophiles with CSO and 37 pedophiles without CSO	NHC: 40	DSM-IV-TR	COM	COM	38.25 ± 8.54 (P+CSO) And 37 ± 8.84 (P-CSO)	36.65 ± 10.13	NA	NA	98 ± 18.87 (P+CSO) and 105 ± 16.65 (P-CSO)	106 ± 18.22	fMRI in combination with go/no-go task	Decreased activation of the medial parietal Cortex in offending pedophiles compared to that of non-pedophiles. No activation difference in prefrontal areas between the two cases.
(Ponseti et al., 2018)	60 male pedophiles	55 male teleiophiles	ICD-10	OC	COM	36.6 ± 10.7	35 ± 10.2	NA	NA	41.5 ± 11.1 (GW)	43.1 ± 9.1 (GW)	fMRI	Pictures of infant animals increased brain activity in the anterior insula, supplementary motor cortex, and dorsolateral prefrontal areas only in pedophiles. Pedophiles also showed an increased brain response to infant animals in the left anterior insular cortex.

Abbreviations (In alphabetical order):
COM: Community; DSM: Diagnostic and Statistical Manual of Mental Disorders; fMRI: Functional Magnetic Resonance Imaging; FPO: Federal probation offices; GW: The reduced version of the German Weschsler Adult Intelligence Scale; HOS: Homosexual; HS: Heterosexual; NHC: Normal healthy control; OC: Outpatient Clinic; P+CSA: pedophiles including a history of child sexual abuse; P–CSA: pedophiles exclusive a history of child sexual abuse; PET: Positron Emission Tomography; T: Tesla, VSS, Visual Sexual Stimuli; WAIS: Wechsler Adult Intelligence Scale, 4th edition; WR: WAIS-R

Table 4. Neuroimaging in paraphilia: A summary of case-series and case-control studies among patients with sadism, violent sexual offenders, and rapist

Study name	Study type	Sample size	Neuroimaging evaluation	Result
(Graber et al., 1982)	Case series	6 mentally ill male sexual offenders, including 3 rapists, 3 pedophilia	CT scan, rCBF	Decreased density measures, decreased blood flow, and performance deficits on the Luria Battery in brain dysfunction in 50% of the sexual offenders.
(Miller, Cummings, McIntyre, Ebers, & Grode, 1986)	Case series	8 patients including hypersexuality (4 cases) or change in sexual preference (4 cases) occurred following brain injury.	CT scan	Disinhibition of sexual activity and hypersexuality followed medial basal-frontal or diencephalic injury.
(Hucker et al., 1988)	Case control	22 sadistic sexual assaulters, 21 non-sadistic sexual assaulters and 36 property offenders	CT scan	More abnormalities in the right temporal horn in sadism.
(Garnett et al., 1988)	Case series	30 years old sadomasochist male and 2 male university students control (aged 23 and 26 years).	PET	More bilateral brain activation among cases.
(Langevin et al., 1989)	Case control	Sadism (n=22), non-sadists (n=21) offender controls (n=36)	CT scan	No significant difference in the overall incidence of gross pathology.
(Aigner et al., 2000)	Case control	96 mentally ill sexual offenders of a high security prison	MRI	More MRI abnormalities in the high violent group as compared to the low violent groups.
(Fruehwald et al., 2000)	Case series	Highly violent incarcerated sexual offenders (n=38).	MRI	A higher rate of minimal brain abnormalities in the highly violent incarcerated sexual offenders.
(Harenski et al., 2012)	Case control	Sadism(n=8), sexual offender- non sadism (n=7)	fMRI	Significant difference in amygdala activation in sadism, significant relation between pain severity rating and activity in the anterior insula.

Abbreviations (in alphabetical order): CT: Computerized tomography; fMRI: Functional magnetic resonance imaging; MRI: magnetic resonance imaging; PET: Positron emission tomography; rCBF: regional cerebral blood flow; SPECT: Single-photon emission computed tomography.

Discussion

Added value of the review

In this review, we summarize all the studies, including case reports, case series, and case controls regarding paraphilia, and categorize them into three major sections: pedophilia, sadism, and other lesions. This review has important clinical and research implications. A wide range of brain lesions in different brain areas were reported in patients with paraphilia; however, most lesions were found in the frontal and temporal lobes (Fig. 2).

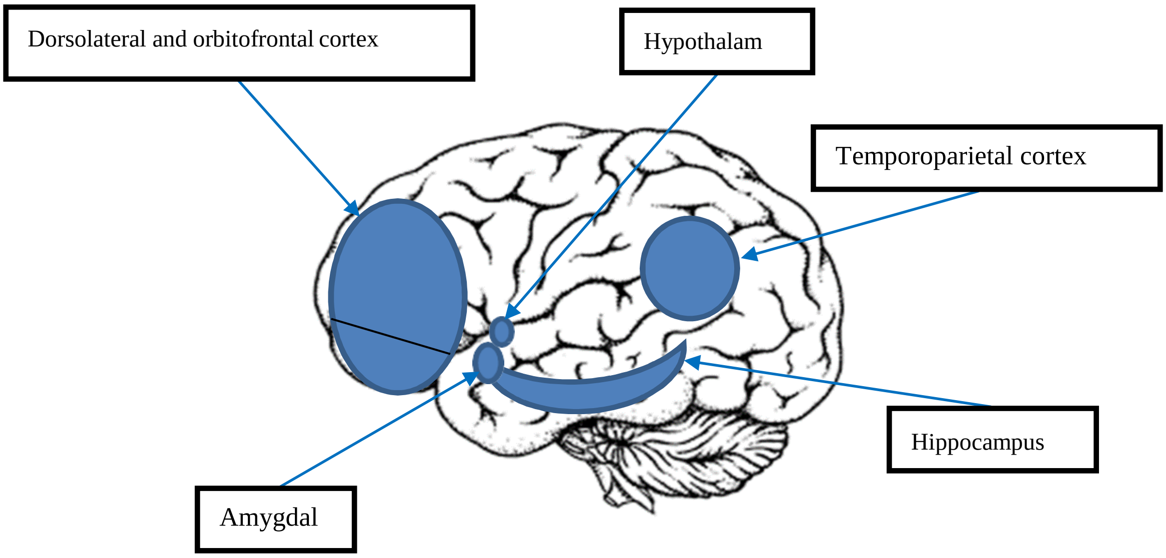

Figure 2. Brain involvements in pedophilia

Based on this review, subjects with acute deviant sexual behavior should be assessed first with structural brain imaging, namely, brain CT scan and MRI. Functional imaging can be used in patients with primary/secondary type of paraphilia; however, the techniques need harmonization.

Neuroimaging and neuroanatomical findings in different types of paraphilia:

Pedophilia

Pedophilia is a complex multifactorial disorder which is probably due to a combination of psychosocial as well as biological factors (8). Initially psychological theories, such as the history of abuse in abusers (9-11), a conditioning hypothesis (12), and negative experiences during childhood, such as serious intra-familial violence (13,14) were proposed as the main causes. However, neurodevelopmental insults, both before and after birth (15-20) and neurodevelopmental factors, such as low intelligence, left-handedness, and smaller stature (21), may also contribute to pedophilia. The first theory of a neurodevelopmental origin of pedophilia was based on limited case reports or case series of sexual disorders after neurological disorders such as dementia, multiple sclerosis, tumor, and epilepsy (Table 1). The first neuroanatomical reports indicated the importance of frontotemporal dysfunctions in pedophilia. In the 1960s and 1970s, a few case reports showed the neurodevelopmental basis of pedophilia (22,23). One of the most interesting cases was reported in 2003 in a man with a history of pedophilia secondary to an orbitofrontal tumor. Despite initial improvements of his symptoms after the tumor resection, he subsequently developed a persistent headache and began secretly collecting pornography. Tumor regrowth was diagnosed in his brain MRI, and he underwent a tumor re-resection (24).

Some studies showed that frontal (24-27) and temporal lobe lesions (28-30) might contribute to pedophilia via disinhibition of sexual behavior (31) and expression of hyper-sexuality. In a psychobiological model of pedophilia, early childhood sexual abuse may also result in neurodevelopmental abnormalities in the temporal and the frontal lobes mediating sexual arousal, erotic discrimination, the cognitive aspects of sexual desire, and behavioral inhibition (32). A meta-analysis on the neuropsychology of sex offenders showed that sex offenders against children demonstrate lower abilities than sex offenders against adults on higher-order executive functions, whereas sex offenders against adults show lower verbal fluency abilities (18). While initially the relationship between anterior brain lesions and violent offending has been shown (33), with more widespread usage of neuroimaging studies, the roles of other parts of the brain have become clear. Using structural neuroimaging techniques, a negative association between pedophilia and white matter volume of the temporal and parietal lobes bilaterally (34), principally in superior fronto-occipital and right arcuate fasciculi, was shown (27). Pedophiles also showed decreased grey matter volume in the left dorsolateral prefrontal cortex (35), the orbitofrontal cortex (27), insular cortex (35), ventral striatum, and even in the posterior and sub-tentorial part of the brain at the cerebellum (27). Lett et al. showed structural brain changes in pedophilic cases with reduced cortical thickness-cortical surface area and white matter fractional anisotropy (36). Smaller amygdala volume has also been demonstrated repeatedly amongst cases with pedophilia (Table 2).

Functional brain neuroimaging studies showed a more complex neural pattern of changes in pedophilia (Table 3). A recent meta-analysis in 58 pedophiles and 65 non-pedophile men did not show significant differences in brain activation between the sexual arousal condition and the neutral condition according to the subject's preferences (37). However, many studies have illustrated that the pattern of brain region activation in patients with pedophilia is quite different from those without.

Using a 7 Tesla STEAM magnetic resonance spectroscopy, Ristow et al. found GABAergic deficits in the dorsal anterior cingulate cortex of pedophilic cases (n= 13), which may support impulsivity theory in pedophilia (38). In pedophilic offenders, a significantly greater activation of the attention network and the right orbitofrontal cortex (39) was shown after the presentation of pictures of boys as compared to the controls. However, the pattern of dysfunction is not necessarily limited to frontal lobe pathology. Interestingly, regions related to the processing of sexual stimuli in normal healthy individuals showed reduced activation during visual erotic stimulation in pedophilic patients (40). In addition, those with pedophilia (both offenders and non-offenders) have a lower activation pattern (n= 15, PET study) in the right inferior temporal cortex than that of normal healthy matched controls (n= 15) (41). These findings emphasize the possible role of the temporal lobe in the region mediating sexual arousal of pedophilic cases.

Moreover, a distinctive pattern of activity has been reported in amygdala (42), orbitofrontal as well as anterior prefrontal regions (43), cingulate gyrus and insular region (44), bilateral anterior insula, anterior temporal cortex, lateral occipital, and the declive of cerebellar vermis (45). While an obvious different pattern of activation can be observed among pedophiles and teleiophiles (Table 3), in a recent study with T1-weighted and diffusion MRI scans of the brain, Gerwin et al. did not find a significant difference between white matter and gray matter in pedophiles and teleiophiles (46). In another study, the neuroanatomy of hebephiles was also more similar to that of pedophiles than that of teleiophiles (47).

In the light of these studies, it may be concluded that a complex neural network, starting from different patterns of activation in brain cortices with special connections to subcortical areas, can be partially responsible for pedophilia. Orbitofrontal and dorsolateral prefrontal cortex lesions may lead to an inhibition deficit (35,48) and consequently may contribute to the sexual assault of children. While prefrontal networks may also be associated with stimulus-controlled behaviors, such as sexual compulsive behaviors (49), hypersexuality due to temporal lobe lesions, the amygdala and hippocampus may also result in sexual preoccupation with children (35,50). A distinctive pattern of sub-cortical/cortical activation (Table 3) may also suggest a network model of striato-thalamic cortical processing in the development of pedophilia (51,52). The result of an fMRI study showed the possibilities of a different moral processing in pedophilic offenders as compared to healthy volunteers (53). Finally, selective activation of the brain region regarding reward and punishment (54), addictive and stimulus-controlled behavior (55) may explain the excessively abnormal interest of subjects toward children, expressed without a sense of fear.

Sadism

Despite the undeniable importance of sadism in the field of forensic psychiatry (56), the reason for this sexual deviance is still a matter of debate. Sadism may be due to "a sense of power and control" resulting from feelings of inadequacy and traumatic experiences in childhood (57,58). Based on the case histories of 16 sadistic rapists in 1983, MacCulloch et al. showed that the majority of sadistic patients had repetitive sadistic masturbatory fantasies, starting during their teenage years (59).

Anterior brain theory, with frontal (23), frontal-temporal and temporal lobe lesions (60), was proposed again based on a few case reports of sadism (Table 1). However, only a few studies used neuroimaging techniques in cases with sadism. Moreover, they used a small sample of sadistic individuals and, more importantly, those with severe violent behaviors and rapists, who may not represent sadism as a whole (Table 4). In a study of six mentally ill male sexual offenders, including three rapists and three pedophiles, Graber et al. showed some degree of brain dysfunction as demonstrated by decreased density measures, decreased blood flow, and performance deficits on the Luria Battery (26).

The result of earlier studies using structural neuroimages varied significantly, from no significant difference in the overall incidence of gross pathology in brain computed tomography (61) to minimal brain abnormalities detected by an MRI (62), such as changes in the right side temporal horn (28) and amygdalohippocampal lesions (63). The result of functional imaging showed a different pattern of brain activation in the right side of the brain (64), amygdala, and insula (65). In a case-control fMRI study of 8 sadists and 7 non-sadists, Harenski et al. showed a high level of connectivity between areas involved in the perception of others' pain (anterior cingulate and anterior insula) and areas associated with sexual arousal (amygdala, hypothalamus, and ventral striatum) (65).

Other types of paraphilia

Only a few studies reported neuroimaging findings in other types of paraphilia. Using single-photon emission in a 24-year-old male with a history of fetishism, a bilateral decrease in cerebral blood flow was observed in the temporal and occipital lobe (66). Although different forms of paraphilia, such as exhibitionism, (22) have been reported in patients with temporal lobe seizures, in a case-controlled study of 15 exhibitionists, and 36 non-violent property offenders, no significant difference was reported in CT scans (61). A case of zoophilia (67) and sexual perversion was reported in a patient with frontotemporal dementia.

In summary, the current literature has remained largely silent in identifying brain involvement in patients with other types of paraphilia, such as exhibitionism and zoophilia. Therefore, further studies are necessary to elucidate the neurodevelopmental basis of such sexual disorders.

Forensic assessment of paraphilia and sexual offenses according to neuroimaging findings

The results of imaging studies may be important for patients, their lawyers, and the judicial system. Few studies reported forensic assessment of patients considering any changes in their brain imaging. In 1972, Lensiak et al. (23) reported a previously healthy man with multidirectional disorders of his sexual drive. According to the first forensic assessment, he was criminally responsible for the index offenses. Further investigation with pneumoencephalography showed a brain tumor. Consequently, the defendant was found not responsible. The case of a fashion writer, Peter Braunstein, with charges of planned kidnapping, sexual abuse, burglary, robbery, and arson shocked society and was a media sensation. While the defendant was found guilty on all charges except arson, the difficulty in forensic assessments started with findings in a PET study, showing a frontal lobe dysfunction (68). Husted et al. reported a young man with multiple neuropsychiatric deficits who was charged with kidnapping and rape. While the imaging studies revealed temporal lobe abnormalities, these lesions were not judicially relevant to defenses (69). A few studies compared the role of neuroimaging in convicted cases. In a case-control functional MRI study (Go/ No-go paradigm), Gibbels et al. did not find any difference in clinical characteristics, neural activation, behavioral/inhibition, and intelligent performance among convicted vs. non-convicted pedophilic cases (70). Neuroimaging findings may have some clinical implications for risk assessments. In a recent MRI study using high-resolution T1-weighted with voxel-based morphometry, Schiffer et al. (71) compared pedophilic cases with a history of child sexual offending (n= 58) vs. those without (n= 60). In this study, the authors found a significant association between a lower grey matter volume in the dorsomedial prefrontal or anterior cingulate cortex and a higher risk of re-offending in child sexual offenders.

In summary, although imaging studies have been used by attorneys as a defense tool, it seems that such findings should be considered only as one piece of documentation for the jury and the final verdict still needs to be made according to whole case histories and the defendants' abilities. The results of recent studies comparing convicted vs. non-convicted cases with paraphilia have welcoming impacts on the neuroanatomical basis of paraphilia; however, the legal implications of these findings need to be re-assessed in further studies. Our study has limitations. A small sample size in the majority of studies and widely heterogeneous methods of assessments did not allow us to perform a meta-analysis. A majority of studies did not report the details of forensic assessments on subjects; therefore, we could not review the role of imaging in forensic assessments thoroughly. The selection of a matched control group in forensic psychiatry studies is often challenging. On the one hand, using offensive controls, even without a clear history of sexual offenses, might be confounded by a possibility of structural and functional imaging abnormalities. On the other hand, adjusting covariates, such as long-term hospitalization in normal healthy volunteers, is impossible. Hence, the best but costliest approach would be to include more than one control group. While a few previous reviews assessed imaging studies in paraphilia, they reported only pedophilia (8,37).

To the best of our knowledge, this is the first study providing a thorough review of major conditions, namely pedophilia, sadism, and other types of paraphilia. Moreover, this paper summarizes the forensic aspects of all neuroimaging studies, from case reports/series to case-control studies. Few studies assess the role of neuroimaging evaluations in paraphilia. However, different research strategies, inclusion/exclusion criteria, and definitions have led to heterogeneous data (8). Multicenter studies with harmonized data may better understand the neuroanatomic aspects of paraphilia. It is also important to provide a clear guideline in the neuroimaging studies necessary for clinical assessments of patients and define their role in assessing the defendant's criminal responsibility. Many cases with late-onset pedophilia have associated neuropsychiatric symptoms and underlying brain lesions. Along with a comprehensive neuropsychological assessment to evaluate neurocognitive functions, such as executive function and verbal intelligence, structural and functional neuroimaging would be useful in assessing such subjects. In addition, changes in the pattern of neuronal responsiveness may also be used to follow the effect of treatment in patients (72).

Conclusion

In summary, a complex model of neuroanatomical networks may be related to paraphilia. Well-designed national/ international studies using neuroimaging techniques are necessary to elucidate the pathophysiology of paraphilia and follow the cases. Despite all methodological differences among neuroimaging studies in paraphilia, these studies may explain the neurodevelopmental basis of such disorders.

Ethical considerations

The authors declare that they have no conflict of interest.

The material contained in this article is a review of previously published or presented data.

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