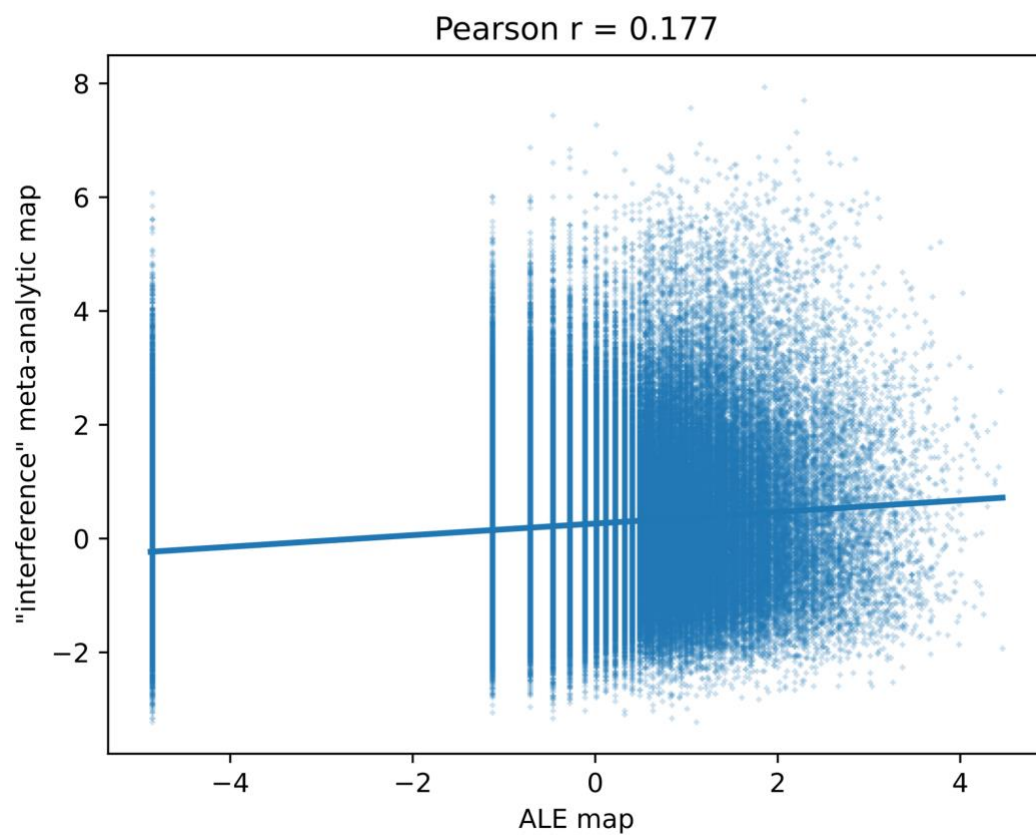


Aberrant brain activity in pedophilia links to receptor distribution, gene expression, and behavior

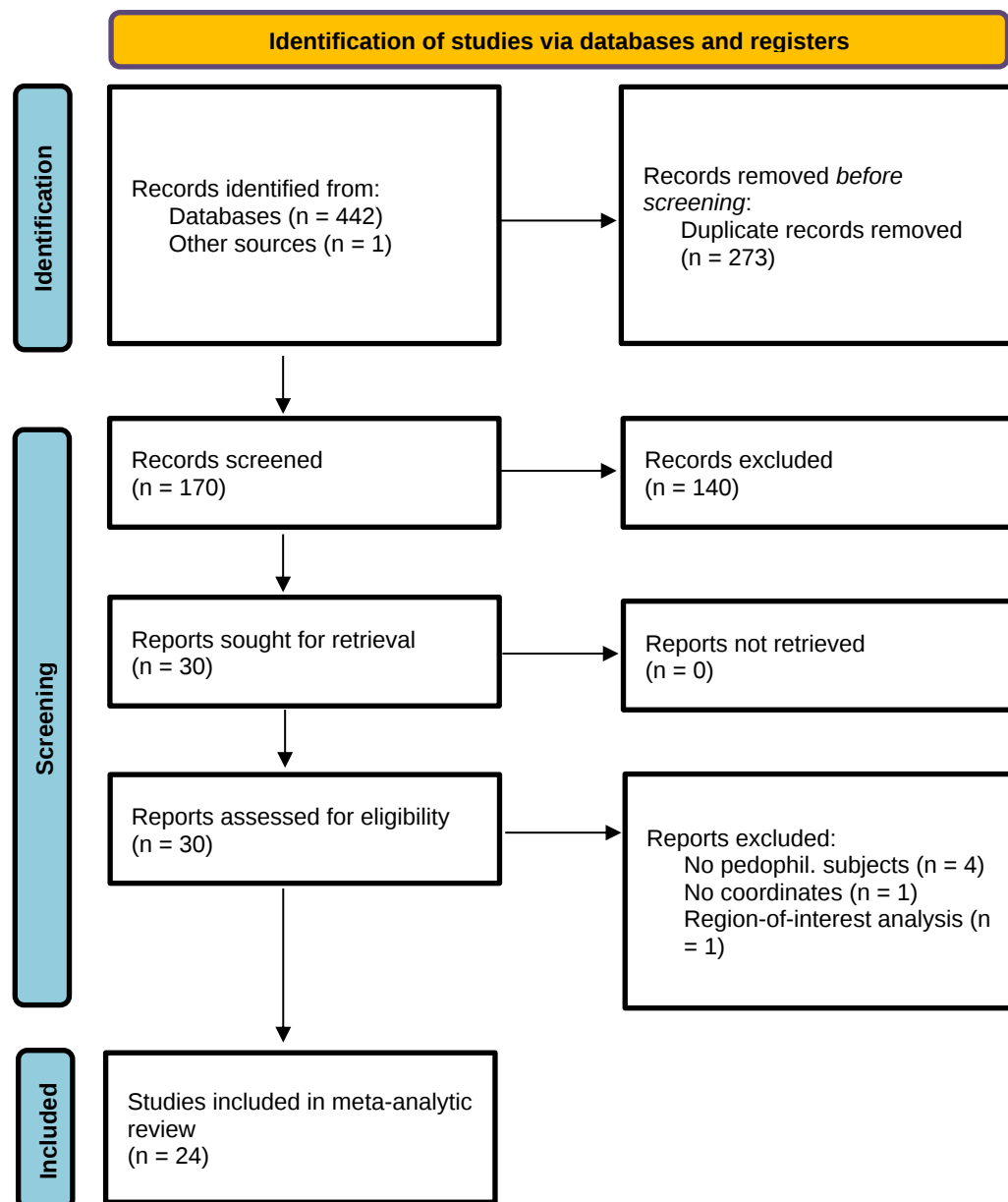
In the format provided by the
authors and unedited

Supplementary Material

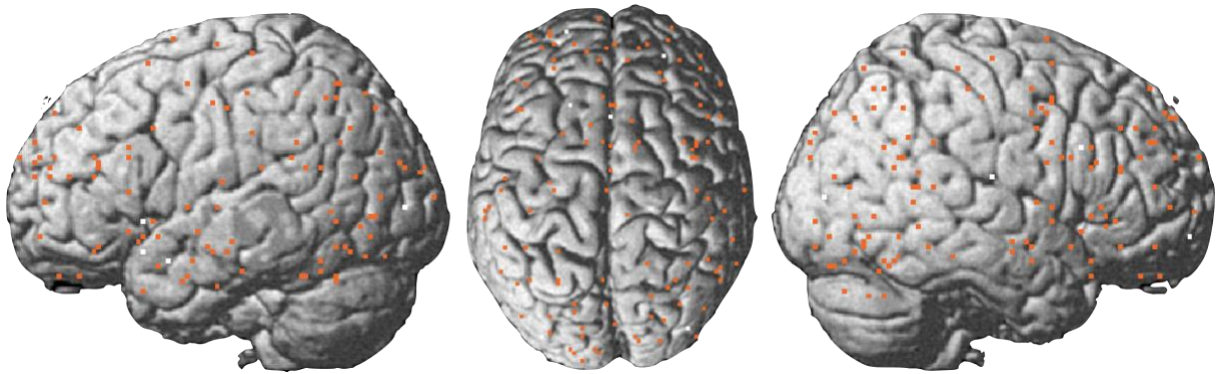
Supplementary Figures



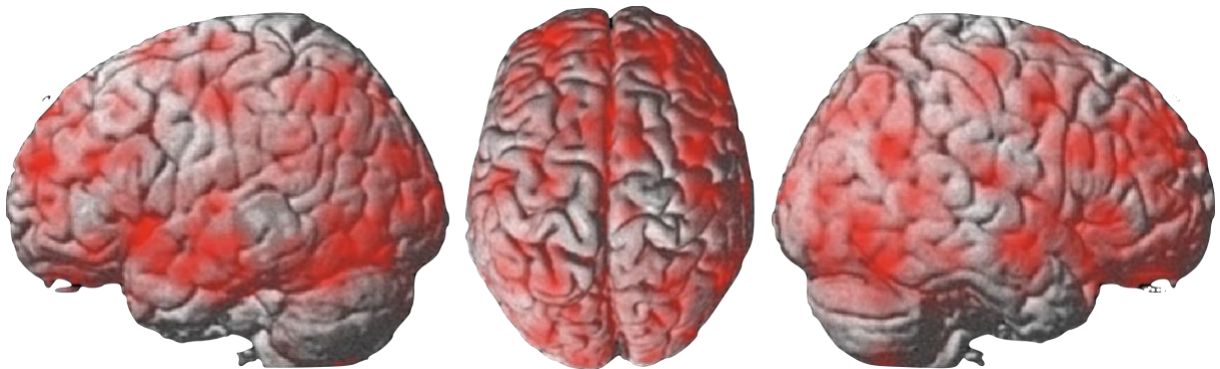
Supplementary Figure 1. Exemplary representation of the correlation of pedophilia-related brain patterns with individual term maps from the Neurosynth database.



Supplementary Figure 2. PRISMA 2020 flow diagram.



Supplementary Figure 3. Summary of the 450 activation foci reported in all 69 experiments included in the meta-analyses.



Supplementary Figure 4. Activation likelihood estimates (ALE), reflecting, for each voxel, the union of the modeled activation (MA) maps across all experiments reporting aberrant brain activity associated with pedophilia.

Supplementary Tables

Supplementary Table 1

Studies reporting neuroimaging experiments indicating alterations in brain activity associated with pedophilia

First author	Year	Subjects		Imaging	Task	Subject-Level Analysis	Group-Level Analysis	Foci	Direction
		<i>Pedophiles</i>	<i>Controls</i>						
Cantor	2016	37	67	fMRI	Rest	Correlation w/ Posterior Default Mode Network	Pedophiles > Controls	17	+
		37	67	fMRI	Rest	Correlation w/ Frontoparietal Network	Pedophiles > Controls	3	+
		37	67	fMRI	Rest	Correlation w/ Frontoparietal Network	Controls > Pedophiles	3	-
		37	28	fMRI	Rest	Correlation w/ Posterior Default Mode Network	Pedophiles > Offenders	18	+
		37	39	fMRI	Rest	Correlation w/ Posterior Default Mode Network	Pedophiles > Non-offenders	3	+
Cazala	2019	25	-	fMRI	Visual Sexual Stimulation	Undressed > Dressed Children	Correlation w/ Pedosexual Desire	1	-
Fontelle	2019	15	15	PET	Visual Sexual Stimulation	Undressed > Dressed Children (Preferred Gender)	Controls > Pedophiles	1	-
		15	15	PET	Visual Sexual Stimulation	Undressed > Dressed Adults (Preferred Gender)	Patients > Controls	1	+
		15	15	PET	Visual Sexual Stimulation	Positive Correlation w/ Desire for Sexual Activity	Pedophiles > Controls	1	+
		15	15	PET	Visual Sexual Stimulation	Positive Correlation w/ Desire for Sexual Activity	Controls > Pedophiles	2	-
		15	15	PET	Visual Sexual Stimulation	Positive Correlation w/ Perception of Erection	Pedophiles > Controls	2	+
		15	15	PET	Visual Sexual Stimulation	Positive Correlation w/ Perception of Erection	Controls > Pedophiles	1	-
		12	10	PET	Visual Sexual Stimulation	Positive Correlation w/ Penile Volume	Pedophiles > Controls	2	+
Habermeyer ^a	2013	8	8	fMRI	Visual Sexual Stimulation	Girls > Women	Pedophiles > Controls	1	+
Habermeyer ^b	2013	11	7	fMRI	Response inhibition	Go <> No-go	Task × Group	4	
Jordan	2014	1	-	fMRI	Visual Sexual Stimulation	Images of Girls	Pre- > Post-Treatment	11	+
		1	-	fMRI	Visual Sexual Stimulation	Images of Girls	Pre- < Post-Treatment	10	-
		1	-	fMRI	Visual Sexual Stimulation	Images of Women	Pre- > Post-Treatment	49	+
		1	-	fMRI	Visual Sexual Stimulation	Images of Women	Pre- < Post-Treatment	8	-
Krylova	2020	17	20	MEG	Visual Sexual Stimulation	P3b response (300–400 ms) for Adult Stimuli	Pedophiles > Controls	1	+
		17	20	MEG	Visual Sexual Stimulation	P3b response (300–400 ms) for Child Stimuli	Pedophiles > Controls	12	+
Kärgel	2015	12	14	fMRI	Rest	Regional Homogeneity	P+CSO > P-CSO	3	+
		12	14	fMRI	Rest	Regional Homogeneity	P-CSO > P+CSO	5	-
Kärgel	2017	37	40	fMRI	Response Inhibition	No-Go > Go	Group × Condition	1	
		37	40	fMRI	Response Inhibition	No-Go > Go	P-CSO > P+CSO	3	-

Mannfolk	ePub	50	54	fMRI	Visual Sexual Stimulation	Children > Adults	Pedophiles > Controls	49	+
Massau	2017	15	19	fMRI	Moral Judgment	General <> Sexual <> Child Sexual Offenses	Group × Condition	1	
		15	19	fMRI	Moral Judgment	Child Sexual > Sexual Offenses	Controls > P-CSO	3	-
Moulier	2012	1	1	fMRI	Visual Sexual Stimulation	Lightly Dressed Boys > Lightly Dressed Girls	Pre- > Post-Treatment, Pedophile	4	+
Poepl	2011	9	-	fMRI	Visual Sexual Stimulation	Tanner I > Tanner V	Regression w/ PPI	3	+
		9	-	fMRI	Visual Sexual Stimulation	Tanner I > Tanner V	Regression w/ PPI	10	-
		9	11	fMRI	Visual Sexual Stimulation	Tanner I > Neutral	Pedophiles > Controls	7	+
		9	11	fMRI	Visual Sexual Stimulation	Tanner V > Neutral	Controls > Pedophiles	1	-
		9	11	fMRI	Visual Sexual Stimulation	Tanner I/V > Neutral	Pedophiles > Controls	5	+
Ponseti	2012	24	32	fMRI	Visual Sexual Stimulation	Nude Men > Boys	Controls > Pedophiles	10	-
		24	32	fMRI	Visual Sexual Stimulation	Nude Women > Girls	Controls > Pedophiles	15	-
Ponseti	2016	24	32	fMRI	Visual Sexual Stimulation	Girls > Women	Pedophiles > Controls	17	+
		24	32	fMRI	Visual Sexual Stimulation	Boys > Men	Pedophiles > Controls	10	+
Ponseti	2018	60	55	fMRI	Nurturing processing	Infant Animals > Adult Animals	Pedophiles > Controls	9	+
Ristow	2019	13	13	fMRI	Expectation	Expectancy of Adult Sexual Stimuli > Fixation	Controls > Pedophiles	3	-
		13	13	fMRI	Expectation	Expectancy of Adult Sexual > Emotional Pictures	Controls > Pedophiles	5	-
		13	13	fMRI	Expectation	(Expectancy of) Child/Adult Pictures	Main Effect of Group	1	
		13	13	fMRI	Visual Sexual Stimulation	Child <> Adult pictures	Stimulus Age × Group	4	
		13	13	fMRI	Expectancy	Expectancy <> Viewing	Condition × Group	1	
		13	13	fMRI	Visual Sexual Stimulation	Expectancy <> Viewing of Child <> Adult Pictures	Stimulus Age × Condition × Group	4	
		13	13	fMRI	Expectancy	Expectancy of Adult > Child Sexual Pictures	Controls > Pedophiles	8	-
		13	13	fMRI	Visual Sexual Stimulation	Viewing of Adult > Child Sexual Pictures	Controls > Pedophiles	7	-
Schiffer ^a	2008	11	12	fMRI	Visual Sexual Stimulation	Nude Boys > Dressed Boys	Pedophiles > Controls	3	+
		11	12	fMRI	Visual Sexual Stimulation	Nude Men > Dressed Men	Controls > Pedophiles	2	-
		11	12	fMRI	Visual Sexual Stimulation	Nude > Dressed Boys/Men	Pedophiles > Controls	3	+
Schiffer ^b	2008	8	-	fMRI	Visual Sexual Stimulation	Nude Girls > Dressed Girls	Correlation w/ Child Sexual Abuse	4	+
		8	-	fMRI	Visual Sexual Stimulation	Nude Girls > Dressed Girls	Correlation w/ Child Sexual Abuse	5	-
		8	12	fMRI	Visual Sexual Stimulation	Nude Women > Dressed Women	Controls > Pedophiles	13	-
		8	12	fMRI	Visual Sexual Stimulation	Nude Girls > Dressed Girls	Pedophiles > Controls	6	+
		8	12	fMRI	Visual Sexual Stimulation	Nude > Dressed Women/Girls	Controls > Pedophiles	12	-
		8	12	fMRI	Visual Sexual Stimulation	Nude > Dressed Girls/Women	Pedophiles > Controls	1	+

Schuler	2022	15	15	fMRI	Cognitive Empathy	Cognitive Empathy > Control	P+CSO > P-CSO	1	+
		15	24	fMRI	Cognitive Empathy	Cognitive Empathy > Control	P-CSO > Controls	1	+
		15	15	fMRI	Cognitive Empathy	Cognitive Empathy > Control	P-CSO > P+CSO	1	-
Stoléru	2013	5	5	fMRI	Visual Sexual Stimulation	Children > Fixation	Pedophiles > Controls	33	+
Szczypiński	2022	11	14	fMRI	Response Inhibition	NoGo > Go	P-CSO > P+CSO	2	-
		11	14	fMRI	Emotional Interference	Negative > Neutral	P-CSO > P+CSO	2	-
Walter	2007	13	14	fMRI	Visual Sexual Stimulation	Erotic > Emotional	Controls > Pedophiles	7	-
		13	-	fMRI	Visual Sexual Stimulation	Erotic > Emotional	Correlation w/ Child Sexual Abuse	4	-
		13	14	fMRI	Visual Emotional Stimulation	Emotional > Neutral	Controls > Pedophiles	3	-
Weidacker	2022	11	8	fMRI	Color-word Stroop Task	Correlation w/ Stroop inference response times	P+CSO > P-CSO	1	+
		11	10	fMRI	Color-word Stroop Task	Errors > Congruent, P+CSO > HC	P+CSO > Controls	2	+
		8	10	fMRI	Color-word Stroop Task	Congruent preceded by error > by congruent	P-CSO > Controls	1	+
		11	8	fMRI	Color-word Stroop Task	Congruent preceded by error > by congruent	P-CSO > P+CSO	3	-

Subjects groups comprised pedophiles and matched controls. The groups of pedophiles included pedosexual offenders (Cantor et al. 2016; Cazala et al. 2019; Fonteille et al. 2019; Habermeyer et al. 2013a; Habermeyer et al. 2013b; Jordan et al. 2014; Krylova et al. 2020; Kärgel et al. 2015; Kärgel et al. 2017; Mannfolk et al., in press; Massau et al. 2017; Moulrier et al. 2012; Poepl et al. 2011; Ponseti et al. 2012; Ponseti et al. 2016; Ponseti et al. 2018; Ristow et al. 2019; Schiffer et al. 2008a; Schiffer et al. 2008b; Schuler et al. 2022; Stoléru et al. 2013; Szczypiński et al. 2022; Walter et al. 2007; Weidacker et al. 2022) and pedophilic non-offenders (Cazala et al. 2019; Fonteille et al. 2019; Habermeyer et al. 2013a; Habermeyer et al. 2013b; Kärgel et al. 2015; Kärgel et al. 2017; Mannfolk et al., in press; Massau et al. 2017; Ponseti et al. 2012; Ponseti et al. 2016; Ponseti et al. 2018; Schuler et al. 2022; Szczypiński et al. 2022; Weidacker et al. 2022). Control groups included healthy controls (Cantor et al. 2016; Cazala et al. 2019; Fonteille et al. 2019; Habermeyer et al. 2013a; Habermeyer et al. 2013b; Krylova et al. 2020; Kärgel et al. 2015; Kärgel et al. 2017; Mannfolk et al., in press; Massau et al. 2017; Moulrier et al. 2012; Ponseti et al. 2012; Ponseti et al. 2016; Ponseti et al. 2018; Ristow et al. 2019; Schiffer et al. 2008a; Schiffer et al. 2008b; Schuler et al. 2022; Stoléru et al. 2013; Walter et al. 2007; Weidacker et al. 2022) and non-sexual offenders (Cantor et al. 2016; Poepl et al. 2011).

Measures of pedosexual interest included the SFDAIS (Stoléru et al. 2011), PPI based on response latencies (Poepl et al. 2011) and MSI subscales (Schiffer et al. 2008b, Walter et al. 2007).

fMRI, functional magnetic resonance imaging; MEG, magnetoencephalography; MSI, Multiphasic Sex Inventory; P+CSO, pedophiles with history of child sexual offense; P-CSO, pedophiles without history of child sexual offense; PET, positron emission tomography; PPI, pedophilic preference index; SFDAIS, Sexual Fantasies, Desires and Activity Interview Schedule.

Supplementary Table 2

Terms involving psychological processes used for behavioral profiling

action	efficiency	intelligence	pain	skill
adaption	effort	intention	perception	sleep
addiction	emotion	interference	planning	social_cognition
anticipation	emotion_regulation	judgment	priming	spatial_attention
anxiety	empathy	knowledge	psychosis	speech_perception
arousal	encoding	language	reading	speech_production
association	episodic_memory	language_comprehension	reasoning	strategy
attention	expectancy	learning	recall	strength
autobiographical_memory	expertise	listening	recognition	stress
balance	extinction	localization	rehearsal	sustained_attention
belief	face_recognition	loss	reinforcement_learning	task_difficulty
categorization	facial_expression	maintenance	response_inhibition	thought
cognitive_control	familiarity	manipulation	response_selection	timing
communication	fear	meaning	retention	uncertainty
competition	fixation	memory	retrieval	updating
concept	focus	memory_retrieval	reward_anticipation	utility
consciousness	gaze	mental_imagery	rhythm	valence
consolidation	goal	monitoring	risk	verbal_fluency
context	hyperactivity	mood	rule	visual_attention
coordination	imagery	morphology	salience	visual_perception
decision	impulsivity	motor_control	search	word_recognition
decision_making	induction	movement	selective_attention	working_memory
detection	inference	multisensory	semantic_memory	
discrimination	inhibition	naming	sentence_comprehension	
distraction	insight	navigation	sex	
eating	integration	object_recognition	sexual	

Supplementary References

- Cantor JM, Lafaille SJ, Hannah J, Kucyi A, Soh DW, Girard TA, Mikulis DJ. Independent component analysis of resting-state functional magnetic resonance imaging in pedophiles. *J Sex Med.* 2016;13:1546–1554.
- Cazala F, Fonteille V, Moulier V, Péligrini-Issac M, De Beaupaire C, Abondo M, Bodon-Bruzel M, Cano J, Cochez F, Fouli T, Thevenon C, Dauba B, Pugeat M, Stoléru S. Brain responses to pictures of children in men with pedophilic disorder: A functional magnetic resonance imaging study. *Eur Arch Psychiatry Clin Neurosci.* 2019;269:713–729.
- Fonteille V, Redouté J, Lamothe P, Straub D, Lavenne F, Le Bars D, Raverot V, Moulier V, Marchand JJ, Vittoz A, Leriche C, Pugeat M, Stoléru S. Brain processing of pictures of children in men with pedophilic disorder: A positron emission tomography study. *Neuroimage Clin.* 2019;21:101647.
- Habermeyer B, Esposito F, Händel N, Lemoine P, Klarhöfer M, Mager R, Dittmann V, Seifritz E, Graf M. Immediate processing of erotic stimuli in paedophilia and controls: A case control study. *BMC Psychiatry.* 2013a;13:88.
- Habermeyer B, Esposito F, Händel N, Lemoine P, Kuhl HC, Klarhöfer M, Mager R, Mokros A, Dittmann V, Seifritz E, Graf M. Response inhibition in pedophilia: An fMRI pilot study. *Neuropsychobiology.* 2013b;68:228–237.
- Jordan K, Fromberger P, Laubinger H, Dechent P, Müller JL. Changed processing of visual sexual stimuli under GnRH-therapy--a single case study in pedophilia using eye tracking and fMRI. *BMC Psychiatry.* 2014;14:142.
- Krylova M, Ristow I, Marr V, Borchardt V, Li M, Witzel J, Drumkova K, Harris JA, Zacharias N, Schiltz K, Amelung T, Beier KM, Kruger TH, Ponseti J, Schiffer B, Walter H, Kärger C, Walter M. MEG reveals preference specific increases of sexual-image-evoked responses in paedophilic sexual offenders and healthy controls. *World J Biol Psychiatry.* 2020;16:1–14.
- Kärger C, Massau C, Weiß S, Walter M, Kruger TH, Schiffer B. Diminished functional connectivity on the road to child sexual abuse in pedophilia. *J Sex Med.* 2015;12:783–795.
- Kärger C, Massau C, Weiß S, Walter M, Borchardt V, Krueger TH, Tenbergen G, Kneer J, Wittfoth M, Pohl A, Gerwinn H, Ponseti J, Amelung T, Beier KM, Mohnke S, Walter H, Schiffer B. Evidence for superior neurobiological and behavioral inhibitory control abilities in non-offending as compared to offending pedophiles. *Hum Brain Mapp.* 2017;38:1092–1104.
- Mannfolk C, Liberg B, Abé C, Rahm C. Altered neural and behavioral response to sexually implicit stimuli during a pictorial-modified stroop task in pedophilic disorder. *Biol Psychiatry Glob Open Sci.* In press.
- Massau C, Kärger C, Weiß S, Walter M, Ponseti J, Hc Krueger T, Walter H, Schiffer B. Neural correlates of moral judgment in pedophilia. *Soc Cogn Affect Neurosci.* 2017;1:12:1490–1499.
- Moulier V, Fonteille V, Péligrini-Issac M, Cordier B, Baron-Laforêt S, Boriassé E, Durand E, Stoléru S. A pilot study of the effects of gonadotropin-releasing hormone agonist therapy on brain activation pattern in a man with pedophilia. *Int J Offender Ther Comp Criminol.* 2012;56:50–60.
- Poepl TB, Nitschke J, Dombert B, Santtila P, Greenlee MW, Osterheider M, Mokros A. Functional cortical and subcortical abnormalities in pedophilia: A combined study using a choice reaction time task and fMRI. *J Sex Med.* 2011;8:1660–1674.

- Ponseti J, Granert O, Jansen O, Wolff S, Beier K, Neutze J, Deuschl G, Mehdorn H, Siebner H, Bosinski H. Assessment of pedophilia using hemodynamic brain response to sexual stimuli. *Arch Gen Psychiatry*. 2012;69:187–194.
- Ponseti J, Granert O, Van Eimeren T, Jansen O, Wolff S, Beier K, Deuschl G, Huchzermeier C, Stirn A, Bosinski H, Roman Siebner H. Assessing paedophilia based on the haemodynamic brain response to face images. *World J Biol Psychiatry*. 2016;17:39–46.
- Ponseti J, Bruhn D, Nolting J, Gerwinn H, Pohl A, Stirn A, Granert O, Laufs H, Deuschl G, Wolff S, Jansen O, Siebner H, Briken P, Mohnke S, Amelung T, Kneer J, Schiffer B, Walter H, Kruger THC. Decoding Pedophilia: increased anterior insula response to infant animal pictures. *Front Hum Neurosci*. 2018;23:11:645.
- Ristow I, Foell J, Kärger C, Borchardt V, Li S, Denzel D, Witzel J, Drumkova K, Beier K, Kruger THC, Ponseti J, Schiffer B, Schiltz K, Walter H, Walter M. Expectation of sexual images of adults and children elicits differential dorsal anterior cingulate cortex activation in pedophilic sexual offenders and healthy controls. *Neuroimage Clin*. 2019;23:101863.
- Schiffer B, Krueger T, Paul T, de Greiff A, Forsting M, Leygraf N, Schedlowski M, Gizewski E. Brain response to visual sexual stimuli in homosexual pedophiles. *J Psychiatry Neurosci*. 2008a;33:23–33.
- Schiffer B, Paul T, Gizewski E, Forsting M, Leygraf N, Schedlowski M, Kruger TH. Functional brain correlates of heterosexual paedophilia. *Neuroimage*. 2008b;41:80–91.
- Schuler M, Mohnke S, Amelung T, Beier KM, Walter M, Ponseti J, Schiffer B, Kruger THC, Walter H. Neural processing associated with cognitive empathy in pedophilia and child sexual offending. *Soc Cogn Affect Neurosci*. 2022;17:712–722.
- Stoléru S, Fonteille V, Moulier V. Neural correlates of pedophilic sexual attraction. *Ann Med Psychol (Paris)*. 2013;171:444–448.
- Stoléru S, Moulier V, Fonteille V, Cazala F. Développement du Questionnaire sur l'intensité des Fantômes, des Désirs et des Comportements Sexuels chez les Auteurs de Violences Sexuelles sur Enfants. In *Cahiers des Résumés, 6e congrès international francophone sur l'agression sexuelle—CIFAS*. 2011, Montreux, Switzerland.
- Szczypiński J, Wypych M, Krasowska A, Wiśniewski P, Kopera M, Suszek H, Marchewka A, Jakubczyk A, Wojnar M. Abnormal behavioral and neural responses in the right dorsolateral prefrontal cortex during emotional interference for cognitive control in pedophilic sex offenders. *J Psychiatr Res*. 2022 ;151:131–135.
- Walter M, Witzel J, Wiebking C, Gubka U, Rotte M, Schiltz K, Bermpohl F, Tempelmann C, Bogerts B, Heinze HJ, Northoff G. Pedophilia is linked to reduced activation in hypothalamus and lateral prefrontal cortex during visual erotic stimulation. *Biol Psychiatry*. 2007;62:698–701.
- Weidacker K, Kärger C, Massau C, Krueger THC, Walter M, Ponseti J, Walter H, Schiffer B. Interference inhibition in offending and non-offending pedophiles: A preliminary event-related fMRI study. *Neuropsychologia*. 2022;173:108301.