Author's response to reviews

Title: Immediate processing of erotic stimuli in paedophilia and controls: a case control study

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Author's response to reviews: see over
Dear Prof. Emmelkamp

Editor of BMC Psychiatry

We are thankful for giving us the chance to revise our manuscript. We are grateful for the careful and accurate revision of our paper and very pleased that the reviewers acknowledged the topic of our study.

We now revised the manuscript according to the reviewer’s insightful suggestions and recommendations. We believe that the constructive comments helped us to improve the quality of our paper significantly.

Please find below a point-by-point list of the reviewer’s comments and our answers and corrections.

**Reviewer 1: Main comments**

The stimulation duration of such paradigms indeed is very important to consider, however, the authors should acknowledge, that at least some studies (which actually have been cited here) applied also short stimuli of only a few seconds. Also I would recommend the authors to elaborate this aspect a little bit in detail, e.g. mention the work by Ferretti et al. Neuroimage 2005; Moulier et al. Neuroimage 2006 and for a discussion of absence or presence of specific erotic activations as an effect of stimulus duration see also Walter et al. Neuroimage 2008.

**Author’s reply**

The reviewer is right. Walter et al. [1] also used a short presentation time. This mistake has been corrected:

“Except for the study of Walter et al. [1] all of the above-mentioned studies that describe a prefrontal involvement in paedophilia used relatively long presentation times ranging from 19.2 - 38.5 s and blocked fMRI designs.”

The reviewer also suggested elaborating the aspect of presentation time. We included the suggested studies and discussed that aspect in more detail:

“Earlier fMRI studies on sexual arousal in normal subjects showed that with shorter presentation times of sexually arousing pictures specific neuronal networks and brain processes can be addressed. Static presentation for 8.75 s as used by Moulier et al. [2] demonstrated for example that the initiation and low levels of penile tumescence are controlled by frontal, parietal, insular and cingular cortical areas. In accordance with these results, Ferretti et al. [3] showed that longer presentation times (> 30 s) induce sexual arousal and penile erection whilst shorter presentation times (< 3 s) induce arousal without erection. A stimulation time of 5 s even allowed to distinguish specific sexual emotional effects from more general emotional effects [4].”
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**Reviewer 1:**

The authors have a very interesting and significant finding in the rOFC, however, given that it is not explained by other main effects, the importance for a specific dysfunction might be questioned. To corroborate their finding, the authors should add to the discussion, that indeed, in another study in pedophilia (Walter et al 2007, Biological Psychiatry), these authors also found deviant activations in the right ventrolateral cortex (with a slightly more lateral peak activation), however, given that nude stimuli of adult females were shown, in this study the pedophile patient group showed reduced(!) activations.

**Author's reply**

We agree that the findings from Walter et al. are important and corroborate our findings. These results are now mentioned in the discussion:

“Further support for a deviant activation in the right lateral OFC can be found in an fMRI study by Walter et al. [1] that revealed a reduced activation for nude stimuli of female adults in paedophilic subjects.”

**Reviewer 1: Minor comments**

p3: You write that a biological model would lead to an optimized therapeutic approach - I am afraid that this is i) not necessarily the case, especially in the light of "intractable" preference (and this is what you investigated, while the treatment rather addresses the behavioral control and ii) a bit too optimistic at the current stage of research.

**Author's reply**

Again the reviewer is absolutely right. We deleted that phrase and added a short phrase to the already existing phrase from the discussion that more or less stated the same notion:

“These results could also be therapeutically relevant as most cognitive behavioural treatment approaches aim to reduce cognitive distortions and the denial of the implications of paedophilic behaviours and to increase the awareness of problematic attraction to children [5] rather than to change the sexual preference.”

**Reviewer 1:**

p6: don't forget to add the version of NBS-presentation - seemingly this was meant to be inserted before submission

**Author's reply**

The version of NBS-Presentation® is now included:
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“… displayed on a personal computer using the Neurobehavioral Systems (NBS) software package Presentation® 12.2. Stimuli were presented via fMRI-compatible digital video goggles (NordicNeuroLab, Bergen, Norway).”

Reviewer 1:

p6: what is the increment for the temporal jitter and why?

Author`s reply

The design was adopted from Bühler et al. [6]. We also used a range between 10-20 seconds. In our study we varied the ISI in steps of full seconds in order to pick up the BOLD signal at different times of the curve.

The missing information is now added:

“While inside the scanner, subjects were presented with various types of pictures in an event related design. We presented 10 pictures from each category (erotic pictures of boys, girls, men, women or neutral control pictures) for 750 ms with a jittered interstimulus interval that varied randomly between 10 – 20 s in steps of full seconds (Figure 1).”

Reviewer 1:

p7: please specify how exactly the cluster threshold was calculated. The small size of 10 voxels using a 0.005 voxel-threshold seems strange to my experience with similar datasets. Please also comment on this aspect. Recently the neuroimaging community has seen some publications with equally small voxel extent thresholds, which later on where found out to be due to inappropriate performance of the correction method, mostly because instead of the smoothness of the residuals, the original smoothing kernel was used for calculation.

Author`s reply

The cluster threshold was calculated exactly as in Forman et al. [7], with the only difference that the smoothness is estimated on a 3D map rather than separately on each single slice 2D map. If we would have used the map obtained from the GLM residuals, the smoothness would have been eventually reduced, leading to even smaller cluster size threshold. This is clearly stated in the paper by Kiebel et al. [8]: “… the method based on the statistical image clearly overestimates the underlying smoothness, if the statistical image contains effects due to an underlying signal …”. Thus, accepting the potential “bias” of estimating the smoothness on the actual statistical map, despite the higher variance of the estimator, always leads to a higher smoothness of the map and therefore to bigger cluster sizes and more conservative thresholds.

In the last version of the paper we maybe did not explained clear enough that we applied the above mentioned procedure to each F-map. That is why we reframed that section.
Moreover we reported now the cluster size for each of the F-maps in the same paragraph:

“To obtain this correction, an uncorrected statistical threshold was initially applied to each of the F-maps at \( p = 0.005 \), and a cluster-level threshold correction procedure based on Montecarlo simulations [7] was applied in order to determine the minimum cluster size below which any activation was to be discarded. This procedure yielded a minimum cluster size of 10 voxels (corresponding to a minimum cluster extent of 280 mm) for the F-maps of the interaction of all factors, 12 voxel (297 mm) for the factor age and 19 voxels (482 mm) for the factor sex.”

Reviewer 2: Main comments:

The statistical analyses appear to have ignored an important point: One cannot conclude that there was no main effect when the interaction term is significant. (Only simple main effects can be tested.)

Author’s reply

The reviewer is correct. It wouldn’t be correct to test for main effects in voxels showing a significant interaction in the three-way ANOVA (two within factors: sex, age and one between factor: group).

We only reported main effects from brain areas outside of the brain region showing this interaction (middle frontal gyrus, aLOFC). The misleading phrases from the results and from the discussion have been corrected. Additionally we included statements that stressed that the described main effects refer only to brain regions that didn’t show such a significant interaction.

In the area that showed the interaction (middle frontal gyrus, aLOFC) only simple contrast and an event related averaging of the BOLD-%-change were calculated in order to show the direction of the effects.

“We found a significant interaction of the factors sex, age and group (\( p < 0.05 \), corrected) in the middle frontal gyrus (Figure 2, Table 2). We furthermore found significant main effects for the factors sex and age outside of the middle frontal gyrus, i. e. in brain areas that didn’t show a significant interaction of all factors.

A significant main effect of the factor sex (female, male) was present at a corrected threshold of \( p < 0.05 \) in the right middle temporal gyrus, right fusiform gyrus, right inferior and middle occipital gyrus and right parietal lobe. In the left hemisphere, the inferior occipital gyrus was also active. We also found bilateral activation in the cerebellum.

The factor age revealed an activation of the right dorsomedial prefrontal cortex (\( p < 0.05 \), corrected).
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For the factor group, no significant activation was found at the latter threshold, but again this finding is restricted to brain areas that did not show a significant interaction of all factors.”

Reviewer 2: Minor comments

The introduction lays out a clear argument for the study; however, two highly important recent studies are missing. Although the manuscript accurately conveys some of the existing (and partly contradictory) fMRI studies of pedophiles, it does not contain or consider the recent meta-analyses of these data (conducted by activation likelihood estimation or ALE). Because such meta-analyses quantitatively summarize the existing findings, their results would be a more relevant description than an qualitative review. At least, the ALE studies should appear prominently in the literature review.

Author’s reply

Reviewer 2 suggested including two recent published meta-analysis of the fMRI studies about pedophilia. We agree that including these meta-analyses would improve the quality of this section. As these papers have to be seen in view of the important work of Stoléru und Redouté we here also added now a short reference to their “neurophenomological model of sexual arousel”. Due to these changes we had to rephrase parts of the introduction:

“In recent years, researchers have increasingly addressed the neuronal underpinnings of sexual arousal in order to better understand sexual behaviour. Stoléru et al. [9, 10] and Redouté et al. [11, 12] were the first to propose a neurophenomological model that disentangled the cognitive, emotional, motivational and physiological components of sexual arousal. Two recently published quantitative meta-analyses on sexual cue reactivity [13, 14] underline that distinctive subcomponents of sexual arousal can be reliably localised by neuroimaging techniques.”

Reviewer 2:

The introduction refers to the DSM-IV definition of paedophilia. There was a change in definition between DSM-IV and DSM-IV-TR; the authors should attend to which was used. Also, the DSM-IV (and DSM-IV-TR) definitions are ambiguous. Although the criteria refer to prepubescent children, the text of the DSM suggests that puberty generally lasts until age 13, which is inaccurate. (Sexual preference for children in puberty is often called “hebephilia.”) The manuscript should indicate exactly how paedophilia was diagnosed.

A more detailed description of the pedophilic sample is warranted. Did they admit to their sexual interests in children? How many victims did they have? Comorbid paraphiliias? Convictions for child pornography?

Author’s reply
The reviewer correctly stresses that the definition of pedophilia is ambiguous and a more detailed description of the study sample is warranted. We now included more details of the clinical characteristics of the paedophilic sample:

“The paedophilic subjects fulfilled DSM-IV-TR criteria for exclusive type (attracted only to prepubescent children) not limited to incest heterosexual paedophilia. Three of the subjects had previously molested prepubescent children, the other five had been convicted because of the possession of large quantities of explicit internet child pornography. Each participant’s sexual orientation and preference for prepubescent erotic stimuli was assessed in a clinical interview, the Multiphasic Sex Inventory (MSI) [15] and additionally verified by the clinical record and the court file. For all subjects, neither the interview nor the record indicated other comorbid paraphilias. None of the subjects had admitted paedophilia prior to the contact with the legal authorities.”

**Reviewer 2:**

The visual stimuli also need to receive greater description. How artificial would they look to anyone else? How were the correct “ages” of the artificial stimuli ascertained? Nude or partly clothed? Solitary images? Doing what?

**Author`s reply**

We included a a more detailed description of the stimuli (please note: examples of the stimuli were included in a figure in the first version of the paper, but the editor asked us to remove these pictures.)

“We presented 10 pictures from each category (erotic pictures of boys, girls, men, women or neutral control pictures) for 750 ms with a jittered interstimulus interval that varied randomly between 10 – 20 s in steps of full seconds (Figure 1). In each picture, only one person of one of the above-mentioned categories was displayed in bathing clothes in front of a plain-coloured background. All pictures showed faces and the complete corpus. Secondary sexual characteristics were clearly visible in the pictures showing adults but were clearly absent in the pictures depicting prepubescent children. We avoided photographs of adolescents and applied a biological rather than a legal cut off to make the pictures of adults easily distinguishable from those of children. Before inclusion into the paradigm rated the study subjects the pictures and only the pictures with the highest ratings on a visual analogue scale were included. Neutral pictures showed simple objects like e.g. a small boot in front of the same background.”

**Reviewer 2:**

Relatedly, the introduction claims that “neuropsychological studies indicated executive dysfunctions in paedophilia” (p. 3). This is a half-truth. There have indeed been studies that have found lower lesser executive functioning, there have also been very many failures to replicate that finding, and many other studies have reported deficits in many other cognitive domains. It would mislead readers to describe the frontal functioning levels as if they were a specific deficit rather than a reflection of a global neuropsychological deficit.
Author`s reply

The reviewer is correct. The criticized phrase simplifies the ongoing discussion about neuropsychological findings in paedophilia way too much. We added some papers showing more generalized neuropsychological findings and clearly stated that until now the literature is conflicting and the findings heterogeneous.

“Findings from neuropsychological studies on paedophilia are heterogeneous. Whilst a lower IQ [16], educational difficulties [17] and a higher rate of left-handedness [18] indicate rather generalized brain dysfunction, other studies suggest more specific alterations like focal weaknesses in frontal-executive [19, 20] and/or temporal-verbal [21] skills or even a more deliberate response style and greater self-monitoring in paedophilic subjects [22, 23]. Furthermore revealed research on personality traits in paedophilia various findings like impaired interpersonal functions, impaired self-awareness, disinhibitory traits, sociopathy and a propensity for cognitive distortions [24]. In summary, it can be stated that the neurobiology of paedophilia remains elusive.”

Reviewer 2:

The parameters of the MRI acquisition sequence do not all appear to be provided and should be added. (TE? FoV? Etc.)

Author`s reply

The missing information has been added:

“First a T1-weighted high-resolution data set that covered the whole brain was acquired using a three-dimensional MPRAGE (magnetization-prepared rapid acquisition gradient echo) sequence with a repletion time (TR) of 2.00, an isotropic spatial resolution of 1.0 mm³, and an echo time (TE) of 3.4 ms. T2* weighted functional images were recorded using echoplanar imaging with a TR of 2500 ms, an isotropic spatial resolution of 3x3x3 mm³ and a TE of 30 ms (FoV 228; matrix 76; spacing between slices: 0.51 mm; interslice time: 69 ms). Altogether 152 volumes with 36 image slices with a thickness of 3 mm were obtained.”

Reviewer 2:

The manuscript repeatedly refers to a “sexual preference” factor. This should probably be called a “sex” factor, as it refers to the sex depicted in the stimuli and not the sexual preference of the study participant.

Author`s reply

We admit that we also struggled to find a good label for that factor. We agree that “sex” is the better choice and changed the label throughout the entire manuscript, tables, legends and figures.
The IQs of the study participants were extremely high. Although this is matched (even exceeded) by the IQ of the control group, it is a potential limit to the generalizability of the findings and merits some comment.

**Author’s reply**

We added a phrase stating this limitation in the discussion:

“In this context it has to be stressed that the IQ of the paedophilic participants can be considered extremely high especially in view of the already mentioned findings from Cantor et al. [16]. Hence we cannot exclude that selection of the study subjects contributed to our findings and that the generalizability of our results might be limited.”

**References:**


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