SUPPLEMENTARY MATERIALS

METHOD

Procedure

Young people who experienced childhood physical abuse were first recruited through social services and psychiatric clinics. Next, for all the abused participants, we requested signed permission from the young people and/or their parents/legal guardian to contact their respective social services to confirm if there were official records of physical abuse. Only participants with formal records were invited to participate in the subsequent interviews and scans. Information from the Childhood Experience of Care and Abuse (CECA) and the Childhood Trauma Questionnaire (CTQ) were consistent with the official records for all but one abused participant who only scored 9 on the CTQ physical abuse subscale. However, there was evidence of severe childhood physical abuse from many other sources, including social services record and in the minimization/denial subscale of the CTQ he scored the maximum score of 3 suggesting that he may be in denial about the abuse. Nonetheless, he was excluded in the final analysis due to large motion artefacts in the scanner.

fMRI Image Acquisition

Gradient echo echo-planar MR imaging (EPI) data were acquired on a 3T GE Signa HDx system at the Centre for Neuroimaging Sciences, Institute of Psychiatry, Psychology & Neuroscience, King's College London. Stimuli were projected on a screen, visible through prism in the scanner.

The body coil was used for RF transmission and an 8-channel head coil for RF reception. During the 9-minute run of the task, in each of 28 non-contiguous planes parallel to the anterior-posterior commissural, 296 T_2*-weighted MR images depicting Blood Oxygen Level Dependent (BOLD) contrast covering the whole brain were acquired with: echo time (TE) = 30ms, repetition time (TR) = 1.8s, 28 slices, flip angle = 75°, in-plane resolution = 3.75mm^2, field of view (FOV) = 240mm, slice thickness/gap = 5/0.5mm, matrix = 64 x 64. A high-resolution gradient echo EPI dataset was also acquired for accurate spatial normalization (TE = 30ms, TR = 3s, 43 slices, flip angle = 90°, in-plane resolution = 1.875mm^2, FOV = 240mm, slice thickness/gap = 3/0.3mm, matrix = 128 x 128).

fMRI Image Preprocessing

Image preprocessing was carried out using Statistical Parametric Mapping software (SPM8, www.fil.ion.ucl.ac.uk/spm). Data were realigned to correct for subject movement and co-registered to the high-resolution gradient EPI, which was then used to estimate the parameters for spatially normalizing the data into a standard anatomical space (Montreal Neurological Institute). The resulting normalized volume time series was spatially smoothed using a Gaussian kernel of 8-mm full width at half maximum.

Morphometric Preprocessing and Analysis

VBM-DARTEL Image Preprocessing

The images were first visually inspected for artefacts and structural abnormalities. Next, a voxel-based morphometry (VBM) analysis (Ashburner and Friston, 2000) was conducted to investigate group differences in gray and white matter volumes using SPM8 software (Statistical Parametric Mapping, Wellcome Department of Imaging Neuroscience, London, UK). The T1-weighted

volumetric images were preprocessed using the VBM protocol with modulation (Ashburner, 2007) where the images were first segmented into gray matter, white matter and cerebrospinal fluid (CSF). DARTEL algorithm was applied to the segmented brain tissues to generate a study-specific template and to achieve an accurate inter-subject registration with an improved realignment of smaller inner structures (Yassa and Stark, 2009). The normalized modulated segmented gray matter and white matter images were next affine transformed into MNI space and smoothed with an isotropic Gaussian kernel of 8-mm at full-width half-maximum, providing a balance between predicted subcortical and cortical effects, and to accommodate the assumptions of Gaussian random field theory and the matched filter theorem.

Global and Region of Interest Brain Volume Analyses

Group differences were evaluated for total gray matter and white matter volumes obtained in the tissue segmentation step of the VBM-DARTEL preprocessing. In a post-hoc region of interest (ROI) approach, regions where groups differed significantly in brain activation were identified and extracted from the anatomical gray matter images using MARSBAR for group comparison to identify whether areas that were functionally different between groups were also structurally different. Total gray matter volume was included as a covariate in the ROI analysis.

RESULTS

Brain Activation

Failed Stop-Go Contrast:

Within-group brain activations

Both healthy and abused groups activated similar clusters of bilateral inferior frontal gyri, anterior cingulate cortex, inferior, middle and superior temporal gyri, supramarginal, inferior parietal, middle occipital and fusiform gyri, cerebellum, right middle, superior frontal gyri and

aleft superior parietal gyri; while abused participants activated additional clusters of bilateral pre-/postcentral gyri, posterior cingulate and inferior occipital cortices, vermis, left hippocampus and precuneus. Psychiatric controls also activated similar but relatively smaller clusters of bilateral inferior and middle temporal gyri, supramarginal, inferior parietal gyri and left superior temporal, middle occipital and fusiform gyri (Table S1 & Figure S2).

TABLE S1. Regions of Activation during Failed Stop versus Go Response Trials for 22 Young People Exposed to Severe Childhood Abuse, 17 Psychiatric Controls and 27 Healthy Controls[a]

Brain Region	BA	Cluster Level		Peak MNI Coordinates[b]	Voxel Level
		No. of Voxels	*p* (corr.)		Z
Healthy Controls					
Right inferior/middle/superior temporal/supramarginal/ inferior/superior parietal/angular/middle occipital/ fusiform gyri	37/19/20/21/37/22/39/40/7	4452	<0.0001	56,-56,40 54,-28,-8 62,-52,0	5.53 5.38 5.26
Left inferior/middle/superior temporal/supramarginal/ inferior/superior parietal/angular/middle occipital/ fusiform gyri	19/37/39/22/40/7	1856	<0.0001	-58,-54,34 -58,-42,38 -50,-64,46	4.88 4.82 4.70
Right lingual/fusiform gyri/cerebellum	19	1425	<0.0001	28,-56,-30 20,-54,-6 28,-44,-22	4.50 4.45 4.43
Right middle/superior frontal gyri	46/10/9/8/6	1195	0.001	22,52,34 14,18,64 16,36,48	5.47 4.71 4.46
Right inferior frontal/middle/superior temporal gyri	47/21/38/22	852	0.005	40,14,-12 34,4,-24	5.44 3.16
Bilateral anterior cingulate cortex /medial frontal gyrus	32/24/9	668	0.014	0,30,24	5.27
Left middle/superior frontal gyri	9/8/10	633	0.017	-30,50,28 -22,46,36	4.93 4.67
Left cerebellum	-	594	0.021	-36,-58,-28 -20,-60,-28	4.16 4.14

Left inferior frontal/superior temporal gyri	47/38	509	0.033	-42,18,-12 -36,2,-18	4.73 3.44
Childhood Abuse					
Left inferior frontal/inferior/middle/superior temporal gyri/ hippocampus/precentral/postcentral/supramarginal/ inferior/superior parietal gyri/precuneus/ inferior/middle occipital/fusiform gyri/cerebellum/vermis	47/44/37/21/20/39/38/22/42/ 6/4/3/1/2/40/7/18/19/36	8536	<0.0001	-32,-54,-30 -50,-74,-6 -42,18,-12	5.93 5.12 5.00
Right inferior frontal/inferior/middle/superior temporal/ precentral/postcentral/supramarginal/inferior parietal/ inferior/middle occipital/fusiform gyri/cerebellum/vermis	47/37/19/21/20/22/39/38/12/ 6/4/2/1/3/40/18	6452	<0.0001	32,-56,-32 62,-52,14 46,18,-8	4.53 5.09 5.06
Left inferior/middle/superior frontal gyri Bilateral anterior cingulate cortex/medial frontal gyrus	46/10/9/8/6/32/24	3065	<0.0001	-34,46,28 -30,42,36 0,32,28	5.83 5.07 4.92
Right middle/superior frontal gyri	10/46/9/8/6	1539	<0.0001	42,40,30 42,8,58 44,44,20	4.48 4.47 4.24
Bilateral posterior cingulate cortices	23/31/24	537	0.029	2,-24,32 -8,-10,34	4.47 3.38
Psychiatric Controls					
Right supramarginal/inferior/superior parietal/angular gyri	40/19/39/7	1204	0.001	48,-62,42 52,-50,38 58,-40,48	4.57 4.14 3.47
Left inferior/middle temporal/middle occipital/fusiform gyri	19/37/21/22/39/18	969	0.003	-44,-72,6 -56,-56,12 -44,-70,-8	4.23 3.99 3.88
Right inferior/middle temporal gyri	37/20/21	617	0.018	58,-32,-6	4.29

				62,-50,-2	4.09
Left superior temporal/supramarginal/inferior parietal/ angular gyri	39/40	591	0.021	-54,-54,34 -40,-58,60 -38,-46,42	4.21 3.47 3.23

[a]MNI= Montreal Neurological Institute; corr=FWE-corrected; BA=Brodmann's Area

[b] For each cluster we present the peak MNI coordinates and the first two subpeaks

TABLE S2. Regions of Activation during Successful Stop versus Go Response Trials for 22 Young People Exposed to Severe Childhood Abuse, 17 Psychiatric Controls and 27 Healthy Controls[a]

Brain Region	BA	Cluster Level		Peak MNI Coordinates[b]	Voxel Level
		No. of Voxels	*p* (corr.)		Z
Healthy Controls					
Right inferior/middle/superior frontal/ superior temporal gyri	47/10/46/9/8/21/22/20/19	22535	<0.0001	52,-60,12	6.45
Bilateral inferior/middle temporal/parahippocampal /	/37/39/36/35/30/4/6/3/1/2			38,46,30	6.37
hippocampus/thalamus gyri	/7/40/19/18			48,-76,10	6.28
Right pre-and postcentral gyri/precuneus					
Bilateral supramarginal/angular/inferior/superior parietal/					
cuneus/inferior/middle occipital/ lingual/fusiform gyri/					
cerebellum					
Right inferior frontal/superior temporal gyri/anterior insula	47/38/12	782	0.015	46,18,-14	5.35
				40,14,-10	5.48
				36,-4,-10	3.35
Left inferior frontal/middle/superior temporal gyri	47/21/38	534	0.045	-40,16,-8	4.99
				-50,2,-22	3.75
				-46,16,-22	3.56
Childhood Abuse					
Bilateral inferior/middle/medial/superior frontal gyri/	46/44/10/9/8/6/32/4/2/1/3	26497	<0.0001	-34,52,24	6.26
anterior cingulate cortex / pre-and	/20/37/19/21/39/22/42/40			40,-50,-24	5.94
postcentral/inferior/middle/superior temporal/	/7/18			-44,-50,-24	5.87
inferior/superior parietal/angular/supramarginal/inferior /					
middle occipital/fusiform gyri/cuneus/ precuneus/					
cerebellum					
Psychiatric Controls					
Right inferior/middle temporal /middle occipital /fusiform	37/19/21/22/39/18/20	1281	0.002	58,-38,-6	4.99

gyri				50,-72,12	4.32
				52,-46,-16	4.26
Left inferior/superior parietal lobules	40/7	972	0.007	-34,-44,42	4.57
				-36,-46,50	4.51
				-34,-52,62	4.21
Right supramarginal gyrus/inferior/superior parietal lobules	40/19/7	811	0.013	32,-68,50	3.77
				36,-46,38	3.65
				44,-54,46	3.62

[a] MNI= Montreal Neurological Institute; corr=FWE-corrected; BA=Brodmann's Area

[b] For each cluster we present the peak MNI coordinates and the first two subpeaks

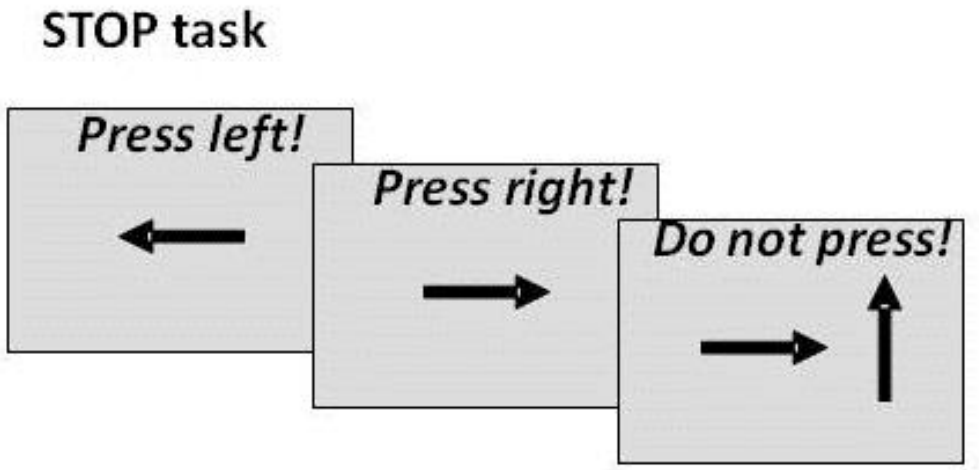
TABLE S3. Correlations between Brain Activation in Dorsomedial Frontal Cortex and IQ, Task Performance, Abuse and Clinical Measures for 22 Young People Exposed to Severe Childhood Abuse, 17 Psychiatric Controls and 27 Healthy Controls[a]

	BOLD Response[b]		
	Healthy Controls	***Childhood Abuse***	***Psychiatric Controls***
IQ	0.07	-0.06	-0.49
Go RT	0.14	0.29	-0.30
Post-error RT	0.15	0.26	-0.06
PA	0.33	-0.22	-0.24
EA	-0.13	-0.41	0.18
SA	-0.02	0.28	-0.30
EN	0.04	-0.15	0.05
PN	-0.21	-0.29	0.03
PA Onset	-	-0.15	-
PA Dur	-	0.17	-
BDI	0.26	-0.08	-0.47
SDQ_Emt	0.20	-0.07	0.06
SDQ_CD	-0.05	-0.42	-0.15
SDQ_Hyp/In	0.01	0.29	-0.51
SDQ_Peer	0.23	-0.18	-0.10
SDQ_Total Difficulties	0.11	-0.11	-0.25

[a] RT=Reaction Time; PA=Physical Abuse; EA=Emotional Abuse; SA=Sexual Abuse; EN=Emotional Neglect; PN=Physical Neglect; Dur=Duration; BDI=Beck's Depression Inventory; SDQ_Emt=SDQ Emotional Problems subscale; SDQ_CD=SDQ Conduct Problems subscale; SDQ_Hyp/In=SDQ Hyperactivity and Inattention subscale; SDQ_Peer=SDQ Peer Problems subscale

[b] Bold response of a spherical region with radius 6mm around the peak voxel (-2,-4, 74)

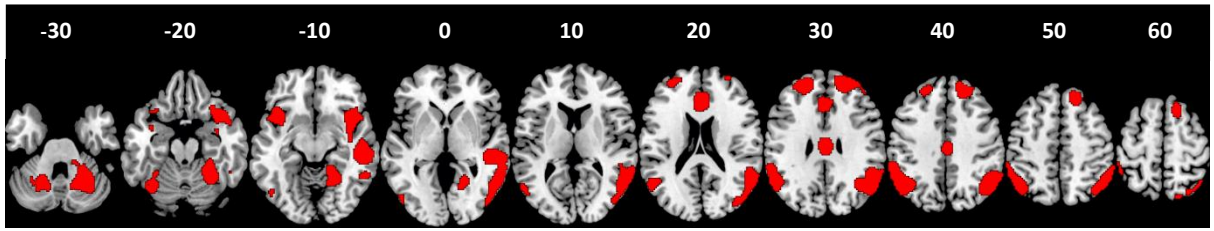
FIGURE S1. Schematic Presentation of the tracking Stop Task



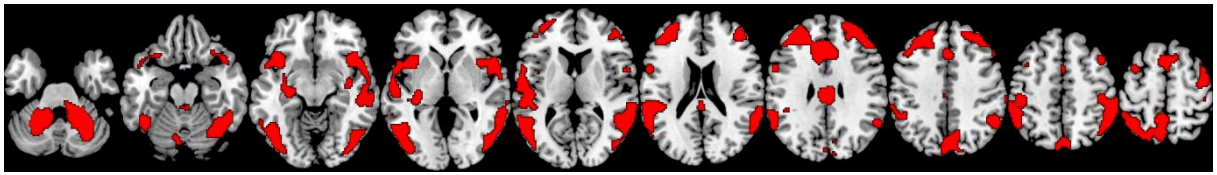
Subjects have to respond to go arrows that point either right or left with a right/left button response. In 20% of trials, the go-signals are followed (about 250ms later) by stop signals and subjects had to inhibit their motor responses. A tracking algorithm changes the time interval between go-signals and stop-signals according to each subject's performance on previous trials (average percentage of inhibition over previous stop trials, recalculated after each stop trial), resulting in 50% successful and 50% unsuccessful inhibition trials.

FIGURE S2. Brain Activation during Failed Stop versus Successful Go Response Trials

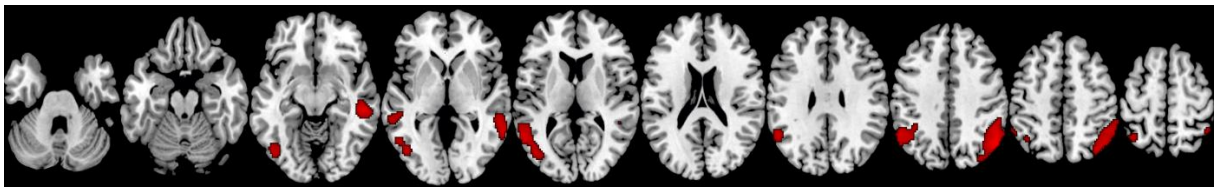
1) Healthy Controls



2) Childhood Abuse



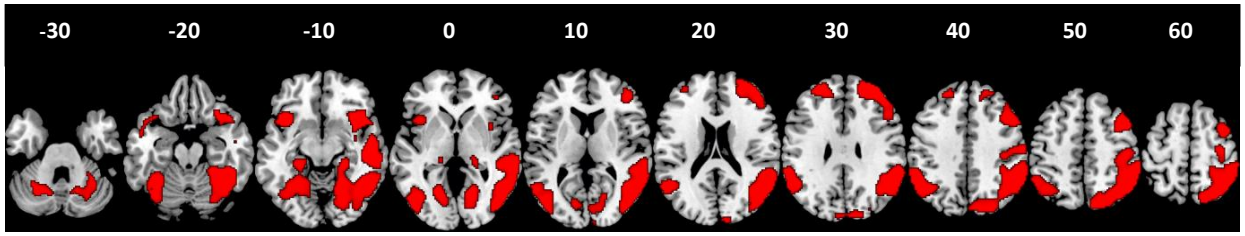
3) Psychiatric Controls



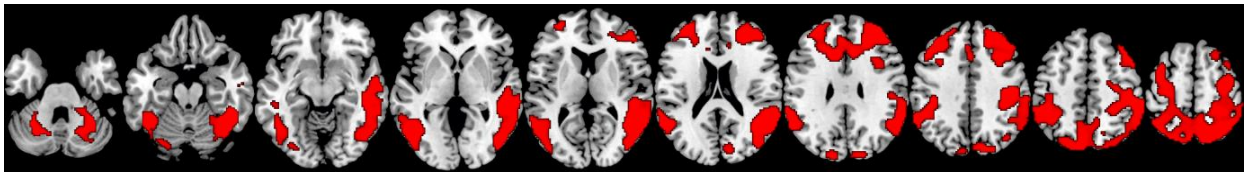
Axial sections of activation during failed stop versus successful go response trials for 1) healthy controls, 2) abused young people and 3) psychiatric controls, $p < 0.05$, FWE-corrected at cluster level. Axial slices are marked with the z coordinate as distance in millimetres from the anterior–posterior commissure. The right side of the image corresponds to the right side of the brain.

FIGURE S3. Brain Activation during Successful Stop versus Go Response Trials

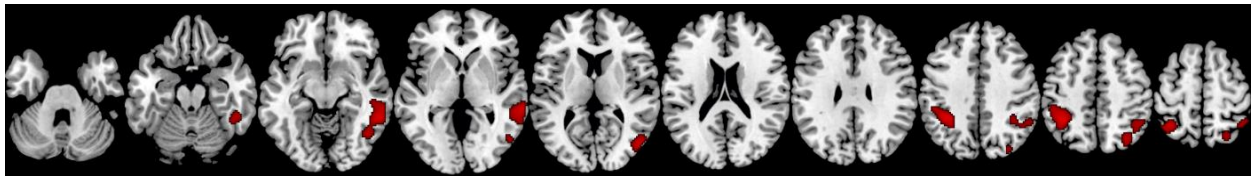
1) Healthy Controls



2) Childhood Abuse

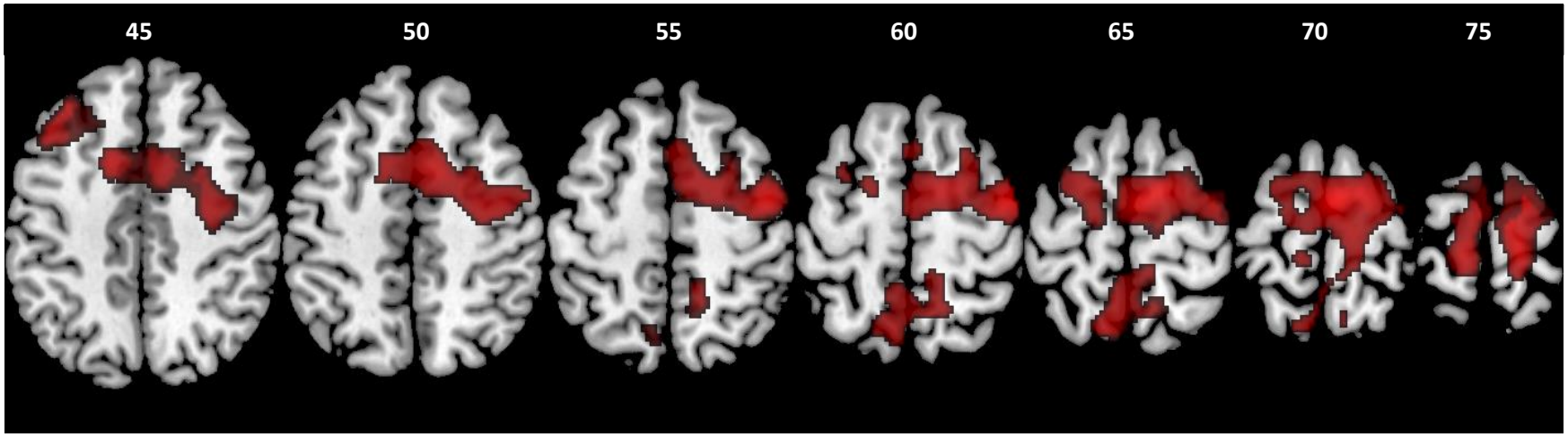


3) Psychiatric Controls



Axial sections of activation during successful stop versus go response trials for 1) healthy controls, 2) abused young people and 3) psychiatric controls, $p < 0.05$, FWE-corrected at cluster level. Axial slices are marked with the z coordinate as distance in millimetres from the anterior–posterior commissure. The right side of the image corresponds to the right side of the brain.

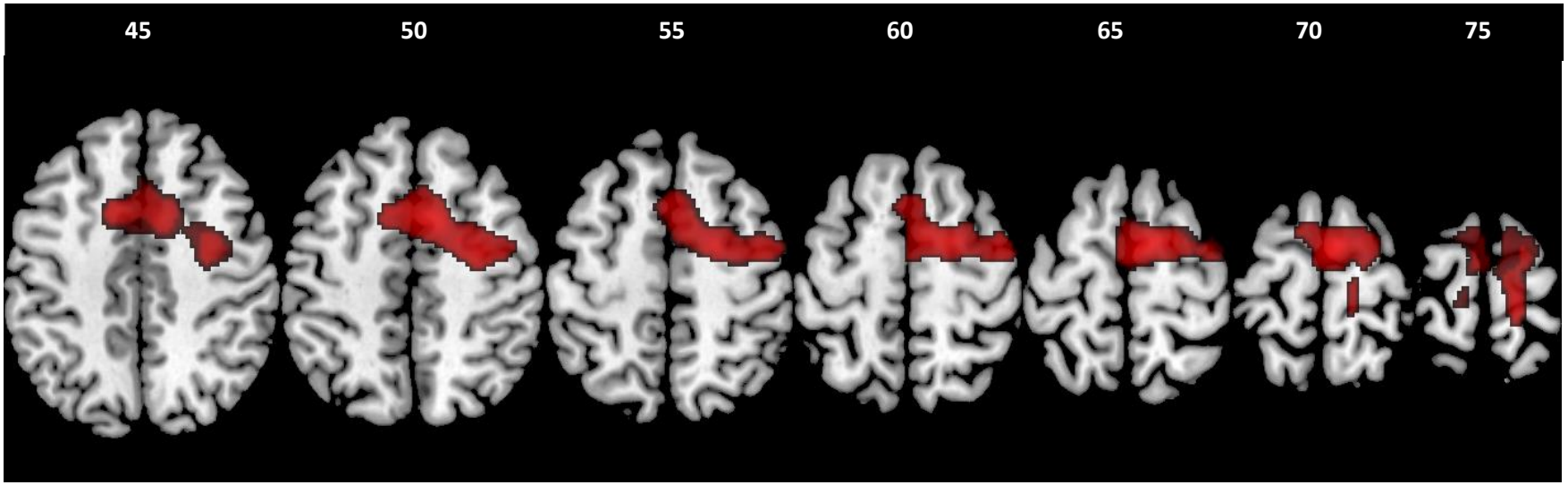
FIGURE S4. Brain Activation during Failed Stop versus Successful Go Response Trials in a Subsample of Abused Young People and Healthy Controls matched on IQ[a]



[a] Axial sections showing increased activation to stop errors relative to successful go trials in a subsample of 22 abused young people compared to 17 healthy controls matched on IQ, $p < 0.05$ FWE-corrected at cluster level. Axial slices are marked with the z coordinate as distance in millimetres from the anterior–posterior commissure. The right side of the image corresponds to the right side of the brain.

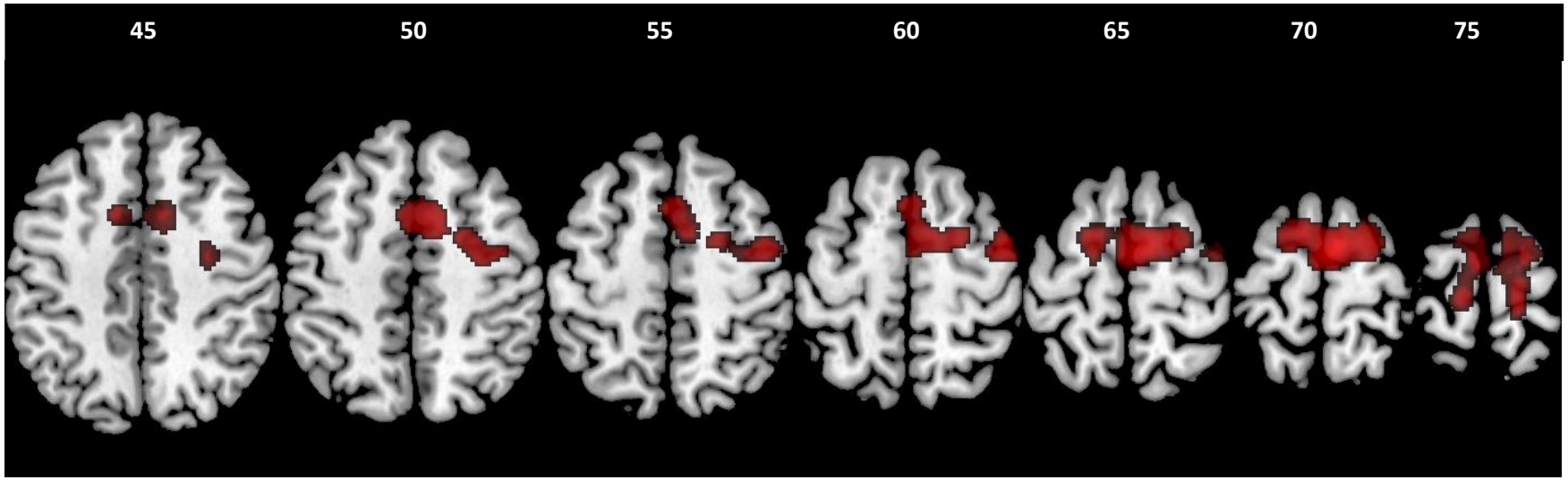
The subgroup of 17 healthy controls had mean (std. deviation) IQ score of 99.8 (8.08); there were no significant group differences in IQ: F (1, 37) =3.9, $p > 0.05$.

FIGURE S5. Brain Activation during Failed Stop versus Successful Go Response Trials in Abused Young People compared to Healthy Controls with IQ as a Covariate[a]



[a] Axial sections showing increased activation to stop errors relative to successful go trials in 22 abused young people compared to 27 healthy controls with IQ as a covariate, $p < 0.05$ FWE-corrected at cluster level. Axial slices are marked with the z coordinate as distance in millimetres from the anterior–posterior commissure. The right side of the image corresponds to the right side of the brain.

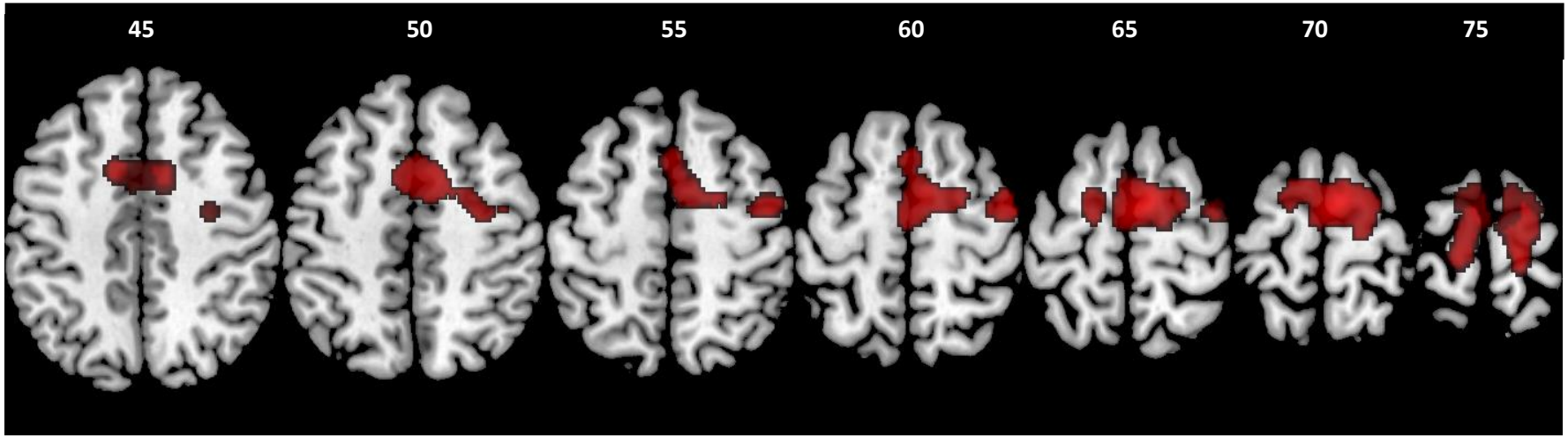
FIGURE S6. Brain Activation during Failed Stop versus Successful Go Response Trials in a Subsample of Abused Young People and Healthy Controls matched on Go Signal Reaction Times[a]



[a] Axial sections showing increased activation to stop errors relative to successful go trials in a subsample of 22 abused young people compared to 23 healthy controls matched on go signal reaction times, $p < 0.05$ FWE-corrected at cluster level. Axial slices are marked with the z coordinate as distance in millimetres from the anterior–posterior commissure. The right side of the image corresponds to the right side of the brain.

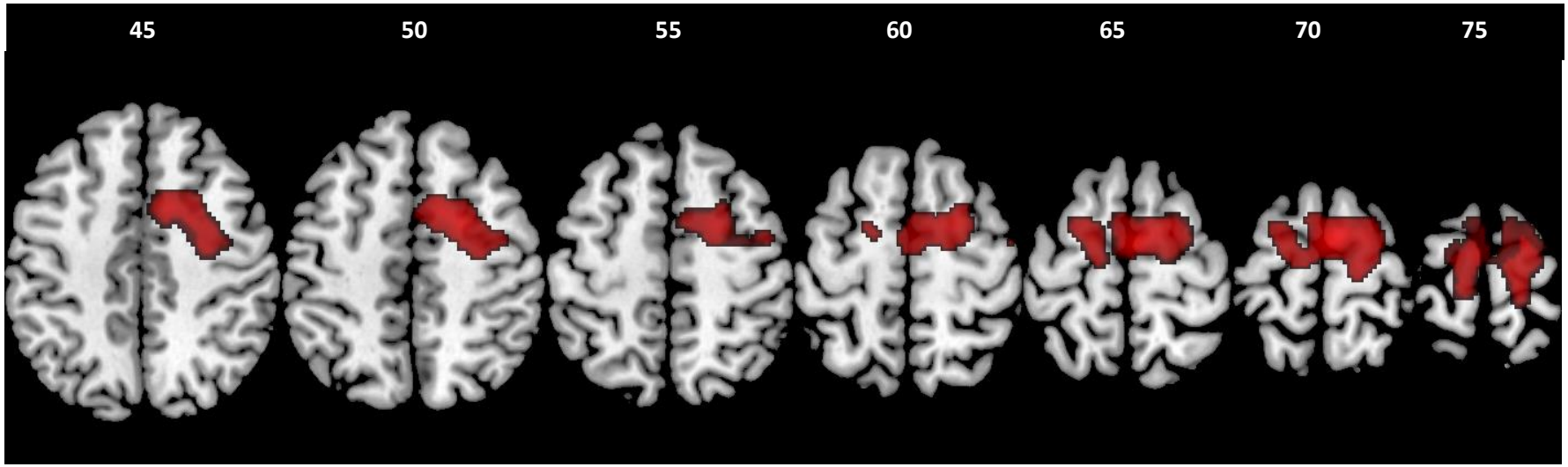
Mean (std. deviation) of go signal reaction times for the subgroup of 23 healthy controls was 507 (77); there were no significant group differences in the mean go signal reaction time: $F(1, 43) = 3.77$, $p > 0.05$.

FIGURE S7. Brain Activation during Failed Stop versus Successful Go Response Trials in Abused Young People compared to Healthy Controls with Post-error and Go Reaction Times as Covariates[a]



[a] Axial sections showing increased activation to stop errors relative to successful go trials in 22 abused young people compared to 27 healthy controls with post-error and go signal reaction times as covariates, $p < 0.05$ FWE-corrected at cluster level. Axial slices are marked with the z coordinate as distance in millimetres from the anterior–posterior commissure. The right side of the image corresponds to the right side of the brain.

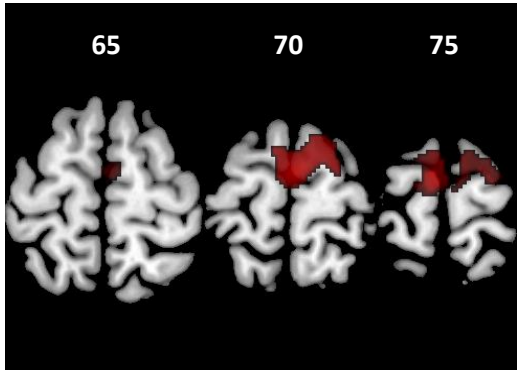
FIGURE S8. Brain Activation during Failed Stop versus Successful Go Response Trials in a Subsample of Abused Young People and Healthy Controls matched on Psychopathology Symptom Scale[a]



[a] Axial sections showing increased activation to stop errors relative to successful go trials in a subsample of 16 abused young people compared to 17 healthy controls matched on the Strengths and Difficulties Questionnaire (SDQ) total difficulties score, $p < 0.05$ FWE-corrected at cluster level. Axial slices are marked with the z coordinate as distance in millimetres from the anterior–posterior commissure. The right side of the image corresponds to the right side of the brain.

Mean (std. deviation) of SDQ total score for the abused group and healthy controls were 15.2 (5.61) and 11.5(3.92), respectively; there were no significant group differences in the SDQ total difficulties score: $F(1, 31) = 4.03$, $p > 0.05$.

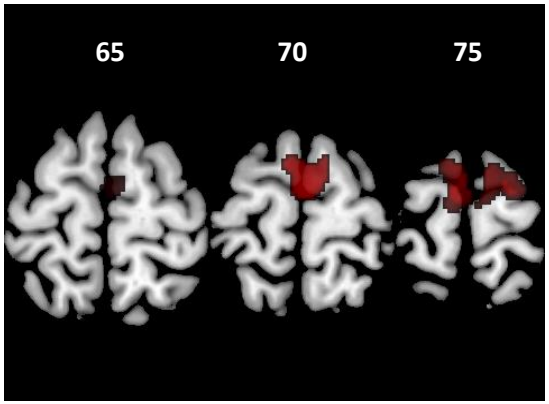
FIGURE S9. Brain Activation during Failed Stop versus Successful Go Response Trials in a Subsample of Abused Young People and Psychiatric Controls matched on the Strengths and Difficulties Questionnaire (SDQ) Conduct Problems Subscale[a]



[a] Axial sections showing increased activation to stop errors relative to successful go trials in a subsample of 16 abused young people compared to 16 psychiatric controls matched on the SDQ conduct problems subscale score, $p < 0.05$ FWE-corrected at cluster level. Axial slices are marked with the z coordinate as distance in millimetres from the anterior–posterior commissure. The right side of the image corresponds to the right side of the brain.

Mean (std. deviation) of SDQ conduct problem score for the abused group and psychiatric controls were 3.44 (1.59) and 2.25 (2.02), respectively; there were no significant group differences in the SDQ conduct problems score: $F(1, 30) = 3.42$, $p > 0.05$.

FIGURE S10. Brain Activation during Failed Stop versus Successful Go Response Trials in a Subsample of Abused Young People and Psychiatric Controls matched on the Strengths and Difficulties Questionnaire (SDQ) Peer Problems Subscale[a]

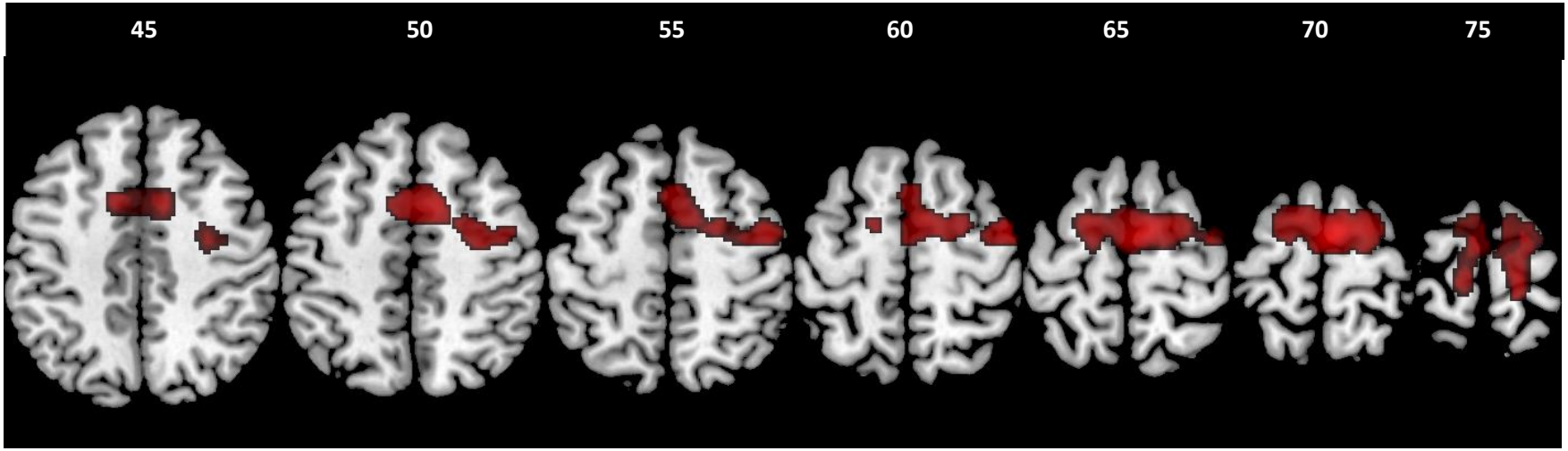


[a] Axial sections showing increased activation to stop errors relative to successful go trials in a subsample of 17 abused young people compared to 17 psychiatric controls matched on the SDQ peer problems subscale score, $p < 0.05$ FWE-corrected at cluster level. Axial slices are marked with the z coordinate as distance in millimetres from the anterior–posterior commissure. The right side of the image corresponds to the right side of the brain.

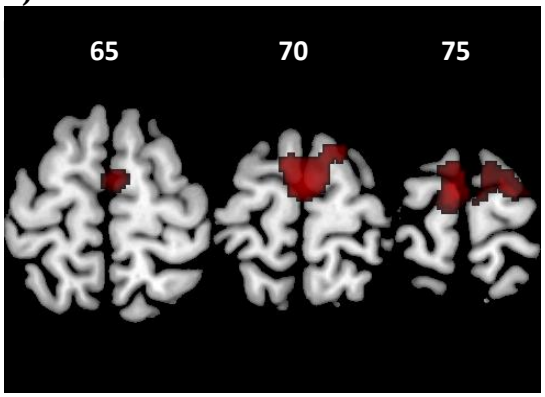
Mean (std. deviation) of SDQ peer problem score for the abused group and psychiatric controls were 3.24 (1.48) and 2.18 (1.78), respectively; there were no significant group differences in the SDQ peer problems score: $F(1, 32) = 3.57$, $p > 0.05$.

FIGURE S11. Brain Activation during Failed Stop versus Successful Go Response Trials in Abused Young People compared to Healthy and Psychiatric Controls with Gender, Ethnicity and Age as Covariates[a]

a)



b)



[a] Axial sections showing increased activation to stop errors relative to successful go trials in 22 abused young people compared to a) 27 healthy controls and b) 17 psychiatric controls; both analyses are conducted with gender, ethnicity and age as covariates, $p < 0.05$ FWE-corrected at cluster level. Axial slices are marked with the z coordinate as distance in millimetres from the anterior–posterior commissure. The right side of the image corresponds to the right side of the brain.

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Yassa MA, Stark CE (2009). A quantitative evaluation of cross-participant registration techniques for MRI studies of the medial temporal lobe. *Neuroimage* 44, 319-327.