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Harsh Corporal Punishment Is Associated With Increased T2 Relaxation Time in Dopamine-Rich Regions

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Abstract

Harsh corporal punishment (HCP) was defined as frequent parental administration of corporal punishment (CP) for discipline, with occasional use of objects such as straps, or paddles. CP is linked to increased risk for depression and substance abuse. We examine whether long-term exposure to HCP acts as sub-traumatic stressor that contributes to brain alterations, particularly in dopaminergic pathways, which may mediate their increased vulnerability to drug and alcohol abuse. Nineteen young adults who experienced early HCP but no other forms of maltreatment and twenty-three comparable controls were studied. T2 relaxation time (T2-RT) measurements were performed with an echo planar imaging TE stepping technique and T2 maps were calculated and analyzed voxel-by-voxel to locate regional T2-RT differences between groups. Previous studies indicated that T2-RT provides an indirect index of resting cerebral blood volume. Region of interest (ROI) analyses were also conducted in caudate, putamen, nucleus accumbens, anterior cingulate cortex, dorsolateral prefrontal cortex, thalamus, globus pallidus and cerebellar hemispheres. Voxel-based relaxometry showed that HCP was associated with increased T2-RT in right caudate and putamen. ROI analyses also revealed increased T2-RT in dorsolateral prefrontal cortex, substantia nigra, thalamus and accumbens but not globus pallidus or cerebellum. There were significant associations between T2-RT measures in dopamine target regions and use of drugs and alcohol, and memory performance. Alteration in the paramagnetic or hemodynamic properties of dopaminergic cell body and projection regions were observed in subjects with HCP, and these findings may relate to their increased risk for drug and alcohol abuse.

Introduction

Corporal punishment (CP) is defined as the administration of physical force with the intention to cause pain but not injury to a child, for the purpose of correction or behavioral control. A quarter of American parents report using harsh CP (HCP) to discipline their 5-12

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year-olds, including spanking with implements, slapping, pinching and shaking. Although the debate over the consequence of CP persists, most studies suggested unfavorable outcomes, including aggression, violence and antisocial behavior, depression, suicidal ideation, anxiety, alcoholism and substance abuse.

Few studies have examined the potential biological consequences of CP. Neuroimaging studies suggest that physical abuse (PA), sexual abuse (SA), and neglect are associated with structural brain changes, including reduced area and fractional anisotropy (FA) of the corpus callosum, hippocampal atrophy, and attenuated gray matter volume (GMV), asymmetry or neuronal integrity in neocortex. Neurobiological changes have also been associated with exposure to types of maltreatment not considered traumatic by the A(1) and A(2) criteria enumerated in DSM-IV. For instance, we reported reduced FA in white matter tracts involved in emotional regulation and language comprehension in young adults exposed to parental verbal abuse. Is it possible that CP may also be associated with changes in brain structure or function? In a separate arm of the present study, we reported reductions in GMV in the right medial prefrontal cortex (MPFC, BA10), left dorsolateral prefrontal cortex (DLPFC, BA9) and right anterior cingulate cortex (ACC, BA24) in subjects exposed to harsh CP. However, functional changes associated with CP remain unknown.

To address this question, we chose to examine a severe and less acceptable form of CP, but to keep it as distinct as possible from physical abuse. The American Academy of Pediatrics (AAP) defines corporal punishment as the striking of a child with an open hand on the buttocks or extremities with the intention of modifying behavior without causing physical injury, as an acceptable but less effective strategy than time-out or removal of privileges for reducing undesired behavior. However, striking a child with an object, such as a paddle, strap or brush, for the same purpose is considered by the AAP to be an excessive, inappropriate and unacceptable means of discipline. Hence, we defined HCP as the chronic, relatively frequent use of physical punishment, often with an implement, for the purpose of disciplining a child, provided it did not extend beyond the buttocks and extremities, was not conducted in a state of overt anger or rage, did not result in physical injury, or fulfill DSM-IV A(1) or A(2) criteria for a traumatic event. These later stipulations were included to differentiate HCP from PA and other forms of traumatic stress. We reasoned that HCP would act as a chronic sub-traumatic stressor and potentially produce discernible effects on brain development. If associations emerged between imaging findings and HCP it would justify studies in a larger group of subjects exposed to ordinary CP, which may be somewhat less stressful.

What are the developmental consequences of chronic exposure to stress? Various studies indicate that early life stress produces enduring changes in stress-regulating systems resulting in increased dopamine and cortisol release in response to subsequent stressors. For example, early stress leads to a reduction in dopamine transporter density and enhances stress-induced dopamine release in nucleus accumbens (NA). Similar alterations appear to accompany exposure to childhood stressors. Pruessner et al. found that college students who experienced low parental care (but not schoolmates with high levels of care) showed a significant release of dopamine in the ventral striatum in response to a mental arithmetic task. Bugenta et al found sensitized hormonal responses to later stressful events in infants who received frequent CP. Hence, we hypothesized that HCP would exert enduring effects on the dopamine system and hypothalamic-pituitary-adrenal (HPA) axis, which could mediate their increased vulnerability to drug and alcohol abuse. The aim of this study was to assess whether HCP was associated with alterations in the ascending dopamine system. Another group of HCP subjects were studied for alterations in HPA response to social stress, which will be reported separately.

T2 relaxometry, a novel, non-invasive, steady-state functional magnetic imaging (fMRI) procedure was used to assess the effects of HCP. We developed this technique to ascertain whether there were alterations in dopamine target territories in children with Attention Deficit Hyperactivity Disorder (ADHD), and found a substantial increase in T2 relaxation time (T2-RT) in the putamen, which correlated with levels of hyperactivity and inattention. T2-RT in the putamen and cerebellar vermis responded to treatment with methylphenidate, suggesting that observed differences were hemodynamic rather than structural. Further, T2-RT in these areas correlated inversely with regional cerebral blood volume (rCBV), as measured by Dynamic Susceptibility Contrast (DSC) MRI. We also found that young adults with a history of SA had elevated T2-RT in their cerebellar vermis. Overall, these studies indicate that T2-RT may serve as a powerful tool for assessing long-term effects of exposure to early stress on the developing brain.

A voxel-based relaxometry (VBR) analysis provided an unbiased and even-handed assessment of major differences in T2-RT throughout the brain, identifying regions of highly significant difference that withstand correction for multiple comparisons. This was followed by an ROI analysis of T2-RT in specific components of the ascending DA system that we hypothesized would be affected by HCP along with contrast regions that we hypothesized would not. We then examined the association between T2-RT in these ROIs and degree of drug or alcohol use.

Methods

Participants

Our goal was to recruit for neuroimaging 20 unmedicated, right-handed subjects (and an equivalent number of unexposed controls), 18-25 years of age from the community who were exposed to HCP but were not exposed to other forms of abuse, trauma or neglect, and whose brain development was not potentially affected by fetal exposure to drugs or alcohol, perinatal or neonatal complications, head trauma with loss of consciousness, neurological disorders (e.g., migraine) or medical disorders that affect growth and development. Subjects were recruited who responded to an advertisement entitled “Memories of Childhood”, and did not know what experiences, disorders, or factors we were looking for as enrollment criteria. They were directed to an online HIPAA-compliant online enrollment system with 2342 entry fields that aggregated a vast array of information regarding their demographics, childhood history, development, and symptomatology. They completed questionnaires on the frequency of open handed spankings, spanking with a belt or stick, hitting/slapping and major means of discipline that took place between ages 1-5, 6-12 and 13-17. Additional surveys provided information on potential exclusion factors including birth and medical history and exposure to other forms of trauma (e.g., PA, SA, motor vehicle accidents, natural disasters, gang violence, muggings, near drowning, animal attacks).

All potentially eligible subjects (e.g., exposed to HCP, but not PA, SA, WDV, PVA or other exclusion factors) were invited in for detailed evaluation, including Structural Clinical Interviews for DSM-IV Axis I and II psychiatric disorders (SCID), supplemented by the ADHD section of the K-SADS-PL. A semi-structured Traumatic Antecedents Interview evaluated the duration and severity of CP and HCP, and confirmed the absence of exposure to other types of childhood maltreatment or trauma. Certified mental health clinicians (Ph.D. psychologists, clinical nurse specialists) conducted the assessment and evaluation interviews. A panel of three doctoral-level psychiatric clinicians with extensive experience treating trauma-exposed children reviewed information on potential subjects and assignments were made by full consensus. HCP subjects were selected without regard to psychiatric history, except for alcohol or drug dependence. Selecting subjects meeting criteria for a specific disorder could bias results by only including the most severely affected

subjects. Conversely, selecting subjects without any psychiatric history could bias results in the opposite direction. We excluded subjects with drug or alcohol dependence as this degree of use would likely affect brain development. Controls were selected to be as similar as possible to HCP subjects in their degree of drug and alcohol use. The intent was to recruit a balanced and representative sample that would provide a rigorous test of our proposed hypotheses.

Subjects were included in the HCP group if they experienced CP to buttocks or extremities by a primary caregiver that began prior to the age of 12, with a frequency of about 12 times or more per year, and were occasionally struck with an implement, such as paddle, belt or hair brush. Such painful physical experience must have been emotionally stressful to the child and extended for a minimum of 3 years. Subjects who were hit on the head or slapped on multiple occasions were excluded to reduce risk that observed effects of CP exposure were due to mechanical injury. Subjects who never received CP or had only minimal exposure (no more than twice a year for 2 years), and were never struck with objects were enrolled into the control group. Half the recruited HCP subjects received MRIs, the other half underwent stress-challenge studies.

Nineteen subjects (13M/6F; mean age 21.8 ± 2.4 years) with HCP and twenty-three age-equivalent controls (12M/11F; mean age 22.0 ± 1.8 years) were imaged. One additional HCP subject underwent neuroimaging but was excluded from this analysis as he had a history of ADHD, which is associated with T2-RT abnormalities in the regions of interest and would have biased results in the predicted direction. The study was approved by the Institutional Review Board of McLean Hospital. All subjects provided written informed consent.

Assessment Measures

Subjects reported their consumption of beer, wine, mixed drinks and shots of hard liquors during typical drinking occasions at college and home as well as the number of episodes of use per month. Consumption was calculated by multiplying the number of drinks consumed per daily drinking session times the number of sessions per month of use. This approach is similar to methods used in epidemiological surveys such as NSDUH. Subjects reported monthly use of street drugs at college and home. These were totaled and expressed as the number of days per month in which drugs were used.

IQ was measured by neuropsychologists using the Wechsler Adult Intelligence Scale – III (WAIS-III). The Memory Assessment Scale (MAS) was used to assess short-term (STM), verbal and visuospatial memory. Self-report ratings of psychiatric symptoms were obtained using Kellner's Symptom Questionnaire (SQ;). The SQ is a 92-item yes/no questionnaire used to elicit four symptom scales (depression, anxiety, anger-hostility, somatization) and four well-being subscales (content, relaxed, friendly, somatic well-being). It was developed to readily detect response to psychotropic medications, and, with the well-being items, is very sensitive to subtle differences from normal. .

Sociodemographic variables are risk factors for drug or alcohol abuse. The two primary components of socioeconomic status (SES) are parental education and income. We used these as separate factors as opposed to combining them into a single SES score, as research suggest that they may have more value as independent covariates. Subjects were often uncertain about parental income, but were well aware of the degree of perceived financial sufficiency, or stress, experienced while growing up. This was rated on a scale ranging from 1 (much less than enough money for our needs) to 5 (much more than enough money for our needs). This measure correlated better with symptom ratings and T2-RT measures than their estimates of parental income and was used instead as a covariate..

Image Acquisition

MRI scans were acquired at the Brain Imaging Center at McLean using a 3T Siemens Trio Scanner. T2 relaxation measurements were performed with an echo planar imaging (EPI) TE stepping technique. We used 8 spin-echo steps, with 16-msec TE increments (e.g. TE (1)=17 msec, TE(2)=33 msec, . . . TE(8)=129msec), and the following parameters (TR=5000 msec, 128×128 matrix on 224 mm FOV, no skip, $1.72 \times 1.72 \times 5 \text{ mm}^3$ voxel size). For each of the steps, there was a refocused spin echo. High-resolution T1-weighted magnetization-prepared rapid acquisition gradient echo (MPRAGE) anatomical images (TE/TR/TI/flip = 2.74 msec/2100 msec/1.1 sec/12 degree, $256 \times 256 \times 128$ matrix on $256 \times 256 \times 170 \text{ mm}^3$ field of view for $1 \times 1 \times 1.33 \text{ mm}^3$ voxel size) were also collected to allow for anatomical localization.

The T2-RT technique employs a non-standard echoplaner TE-stepping protocol to provide a measure of T2 decay with sufficient accuracy and reproducibility that it can be used to detect hemodynamic or other fluid dynamic changes. Contributions to T2 include pure T2 [spin-spin] effects, and perfusion and diffusion processes in the presence of microscopic susceptibility, such as provided by blood. The last contribution is a T2* effect but is not reversible by a spin echo and so can be measured by spin echo T2-relaxometry. We have proposed that T2-RT can serve as an indirect non-invasive index of rCBV. A mono-exponential intensity decay curve $M(t) = M_0 e^{-t/T2}$ was generated across TE times, and the calculated decay constant provides a measure we refer to as T2-RT. The relationship between T2-RT and rCBV is based on the premise that, at steady state, a close coupling exists between regional metabolism and blood volume, on the one hand, and a constant level of oxygen extraction and deoxyhemoglobin concentration ([dHb]), on the other. Thus, regional [dHb] depends directly on rCBV. This is important as [dHb] is the most significant dynamic factor influencing regional paramagnetic properties. We found a substantial inverse correlation between T2-RT and rCBV using dynamic susceptibility contrast (DSC).

Preprocessing procedure

Voxel-based relaxometry (VBR) followed methods described by Pell et al and Mueller et al. First, stepped-EPI images were motion corrected using *mcflirt* in FSL, and the signal intensity for each voxel across TE was fit to a mono-exponential decay curve to generate voxel-wise T2 maps using an in-house *FMRI Analysis Tool* (FAT). T1-weighted structural image was co-registered to the subject's T2-weighted image (TR=5000s, TE=81ms), followed by a unified segmentation and spatial normalization procedure implemented in Statistical Parametric Mapping 5 (SPM5) to generate modulated gray matter, white matter and CSF images in standard Montreal Neurological Institute (MNI) space. The resulting transformation matrix was used to spatially normalize the T2 map into standard space. All T2 maps were resampled at $2 \times 2 \times 2 \text{ mm}^3$. Subsequently, a tissue mask that consisted of both modulated gray and white matter images was combined and thresholded at 0.5, then applied to the normalized T2 map to reduce CSF partial volume effect. Finally, the resulting T2 map was smoothed with an anisotropic Gaussian kernel at $4 \times 4 \times 10 \text{ mm}$ (FWHM), to compensate for the reduced sensitivity in the z direction of the original images.

Data Analysis

2.1. Voxel-based relaxometry analysis—Normalized T2 maps were analyzed using SPM5 and Matlab 7.0 (The Mathworks, MA, USA). Two-sample *t*-test was used to detect voxel-wise differences in T2-RT between HCP and controls. Grand mean scaling was applied and an ANCOVA model was used that controlled for global intensity, gender, age, and perceived financial sufficiency. A smoothed ($4 \times 4 \times 10 \text{ FWHM}$) group mask was used, and only voxels falling within the group mask were included in the analysis. Group comparisons of HCP versus control (HCP > control) and control versus HCP (control >

HCP) were performed using GLM and corrected for multiple comparisons at cluster level P corrected < 0.05 .

2.2 .Region of Interest (ROI) analysis—ROI analyses were conducted to confirm VBR result using hand measures and to specifically quantify T2-RT in key components of the ascending dopamine system, including caudate, putamen, NA, DLPFC, ACC, and thalamus. The substantia nigra (SN) was included to ascertain if HCP was associated with alterations in T2-RT in cell body regions. The internal globus pallidus (GPi) and cerebellar hemispheres were included as contrast regions that receive minimal or no direct dopamine innervation. Drawings of subcortical ROIs on the normalized mean structural image were guided by the Talairach Daemon database atlas. The dorsal ACC was outlined according to the location specified in a meta-analysis study. The DLPFC ROI was a 10 mm diameter sphere (MNI: $X = \pm 22$, $Y = 20$, $Z = 44$) centered on the region of dopamine release during performance of executive function tasks. The cerebellar hemisphere ROI was a 30 mm diameter sphere centered at MNI: $X = \pm 30$, $Y = -62$, $Z = -49$. ROIs were applied to the normalized unsmoothed T2 maps to extract median T2-RT values.

MANCOVA was used to detect group, hemisphere and group $\times$ hemisphere differences. Covariates included age, gender, parental education and perceived financial sufficiency, provided that the covariate had a meaningful regressive relationship ($p < 0.2$) with the dependent variable.

We then sought to test the hypothesis, in all subjects, that T2-RT measures in our primary regions of interest (excluding contrast regions) correlated with degree of drug and alcohol use regardless of cause (e.g., HCP, low SES, family history). T2-RT values in each ROI were normally distributed by Kolmogorov–Smirnov criteria. Degree of drug and alcohol use were log-transformed to better normalize their distributions. Partial correlation analysis controlled for age and gender. We used the false discovery rate method of Benjamini and Hochberg to minimize the risk of type I errors in multiple comparisons. This method rank-orders observed p -values and only accepts those above a critical threshold as significant in order to limit the overall False Discovery Rate, which was set as $p < 0.05$ to balance Type-I and Type-II risk in an exploratory analysis. General statistical analyses were performed using PASW software version 17.0 (SPSS Inc., Chicago, IL).

Results

Demographics and neuropsychological measures

As summarized in Table I, controls and HCP subjects were 22 ± 2 years old on average. They had completed about 2 years of college studies and did not differ in verbal, performance and full-scale IQ. Mean IQ scores were typical for college students. They also did not differ significantly in memory performance, though there was a trend-level difference of 8 points in short-term memory ($p = 0.06$). Parents of HCP subjects had 1.6 ± 0.7 fewer years of school. Subjects in the HCP group also reported a slight but significant decrease in perceived household financial sufficiency during childhood. Exposure to HCP began early (4.3 ± 2.3 years) and persisted for an average of 8.1 ± 3.5 years. HCP subjects had slightly elevated ratings of depression and somatization. Three of the HCP subjects had a past history of major depression including one with comorbid generalized anxiety disorder and two in partial remission. There were single subjects with bipolar disorder, past history of cannabis abuse and past history of alcohol abuse. Three of the subjects with mood disorders, including the subject with bipolar disorder and two with major depression in partial remission, had clinically-significant ratings of depression at the time of assessment. Twelve of the HCP subjects (63%) had no history of Axis I or II disorders. These findings are

consistent with past observations showing that HCP is a risk factor for depression and substance use disorders.

VBR analysis result

There were two clusters of increased T2-RT in the HCP group, which were located in right caudate (MNI: $x = 18$, $y = 20$, $z = 6$, cluster size = 118 voxels, corrected $P = 0.004$) and right putamen (MNI: $x = 32$, $y = -6$, $z = 6$, cluster size = 82 voxels, corrected $P = 0.036$) (Fig 1). There were no significant clusters of increased T2-RT in controls. T2-RT in the caudate cluster, and to a lesser degree in putamen, correlated inversely with measures of short-term, visual and global memory across all subjects (Table II). Interestingly, this association was apparent in HCP subjects but not controls (e.g., caudate cluster and global memory: HCP $r = -0.732$, $p = 0.002$; controls $r = -0.255$, $p > 0.3$). There were no significant correlations between T2-RT in these clusters and degree of alcohol or drug use.

ROI analysis results

T2-RT was significantly higher in HCP subjects than controls in caudate, putamen, thalamus, SN and DLPFC (Table III). There were significant group $\times$ hemisphere interactions in NA and SN, resulting from unilateral HCP > control differences in T2-RT on the right side. A significant group $\times$ hemisphere interaction in putamen was associated with a slight but consistent difference in laterality (T2-RT control: $R > L$; HCP: $L > R$). As expected, there were no group or group $\times$ hemisphere differences in GPi or cerebellar hemispheres.

There were significant correlations between frequency of drug use and T2-RT in bilateral DLPFC and ACC across all subjects (Table IV). There were also significant correlations between T2-RT in these regions and number of alcoholic drinks imbibed per month. Interestingly, in controls the strongest associations involved ACC (e.g., Drug Use: ACC $r = 0.648$, $p = 0.001$; DLPFC $r = 0.407$, $p < 0.07$). Conversely, in HCP subjects the strongest associations were with DLPFC (e.g., Alcohol Use: ACC $r = 0.405$, $p = 0.11$; DLPFC $r = 0.529$, $p < 0.03$).

Discussion

In this study we provide the first evidence that HCP may be associated with enduring alterations in hemodynamic or paramagnetic properties of the right caudate and putamen. T2-RT in these clusters was significantly associated with memory performance suggesting functional consequences. The observation that T2-RT correlated strongly with memory performance in HCP subjects but not controls is interesting if it can be confirmed through replication. One potential explanation is that controls have a healthy reserve capacity and can enhance neuronal activity and blood flow in these regions to the extent necessary to perform memory tasks. In contrast, functional activity in these regions may be impaired in subjects exposed to HCP, with the extent of the deficit reflected in the degree of elevation in T2-RT. Those with the greatest deficits may have the lowest reserve and the most limited capacity to augment activity and blood flow during memory tasks, and hence the poorest performance.

ROI analyses revealed group differences in T2-RT in caudate, putamen, thalamus and DLPFC bilaterally, and in right SN and NA. Trend level differences falling short of significance were also observed in the ACC. There were no differences in T2-RT in GPi and cerebellar hemispheres, which were selected as regions with minimal or no significant dopaminergic innervation. The GPi is innervated primarily by non-dopaminergic fibers from the striatum, which travel by either a direct pathway or through an indirect pathway

involving the external globus pallidus and the subthalamic nucleus. There is however in primates a secondary nigropallidal pathway that is relatively spared in Parkinson's disease. The vermal portion of the cerebellum has receptors and transporters for dopamine but the hemispheres appear to be essentially devoid of dopamine fibers. The thalamus is poorly innervated by dopamine fibers in rats, but is richly innervated in human and non-human primates.

Meaney and colleagues reported that exposure to early stress decreased density of dopamine transporters in the NA of rats, and increases their degree of dopaminergic and behavioral response to stress and psychostimulants. Similarly, we found in rats that early stress decreased dopamine fiber density in the shell but not the core of NA. Preclinical studies indicate that corticosterone and/or corticotropin-releasing hormone (CRH) exert effects on the mesocorticolimbic DA system, causing an increase in dopamine release, which may be critical for stress-induced sensitivity to drugs and to the phenomenon of craving. Hence, early exposure to HCP could act as a chronic sub-traumatic stressor, which may increase susceptibility to substance abuse by altering the developmental trajectory of the ascending dopamine system. However, in contrast to the preclinical studies, differences observed in HCP subjects involved both the mesocorticolimbic and nigrostriatal systems.

The correlation between T2-RT and degree of drug and alcohol use by HCP subjects is plausible. We previously observed increased T2-RT in the putamen of hyperactive children with ADHD, who are at increased risk for developing substance abuse disorders. (No subjects with ADHD were included in this analysis.) Cortical regions identified in this study have been found in prior studies to be associated with craving, drug addiction, and alcohol abuse. One possibility is that diminished steady-state dopaminergic activity in these regions may lead to a deficiency state that is alleviated by drugs of abuse. Individuals with this deficiency may be particularly likely to seek out and use drugs or alcohol, and to experience cravings in their absence. Correlations between T2-RT and drug and alcohol use were seen in both HCP subjects and controls, though correlations in subjects with HCP were more specifically localized to the DLPFC, whereas in controls they were stronger with ACC. Degree of drug and alcohol use is likely the consequence of a large number of experiential, interpersonal and hereditary factors. Although controls were selected for this study who used drugs and alcohol at rates similar to HCP subjects, they may do so for different psychological or neurobiological reasons.

A growing body of literature suggests that the striatum plays a role in cognitive processes such as working memory, reasoning and attention. The strongest relationship between T2-RT and memory performance was in the right head and body of caudate. This is the most anterior aspect of the caudate and it receives direct input from DLPFC, a region known for its role in spatial working memory. Dopamine plays an important role in working memory, and is released in human prefrontal regions during both visual delay, and verbal working memory tasks. Hence, observed associations between memory and T2-RT in DLPFC and striatum seem plausible. However, since the correlation was only observed in subjects with HCP it should be interpreted with caution.

The present findings of increased T2-RT in DLPFC bilaterally and in right ACC of HCP subjects are reasonably consistent with our prior observations of reduced GMV in left DLPFC, (BA9) and right ACC (BA24). However, the present study also identified abnormalities in striatal and thalamic regions not identified by VBM.

The study is limited by the relatively modest sample size, and by slight but significant group differences in sociodemographic factors that were controlled for statistically. T2-RT is also a complex measure. While we have shown that T2-RT correlates with rCBV, and is

influenced by methylphenidate, it is not a purely a hemodynamic or functional measure. VBR has primarily been used to assess subjects with temporal lobe epilepsy who frequently show abnormal elevations of T2-RT in hippocampus and parahippocampal gyrus. While we suspect that T2-RT differences in striathalamic regions, and possibly cortex, reflect differences in deoxyhemoglobin content, these findings will need to be confirmed using alternative techniques such as arterial spin labeling (ASL) or DSC. ASL may currently lack the signal-to-noise sensitivity needed to detect the small but highly significant differences discernible using T2-relaxometry.

We must emphasize that an association between HCP and alterations in T2-RT does not imply causality. Although these subjects did not meet past or present criteria for ADHD, or have higher ratings of aggression, the current finding of increased T2-RT in BA24, and our previous finding of reduced GMV in BA10 may suggest an alternative interpretation. It seems logical that children may increase their risk of exposure to CP or HCP if they have an inadequate ability to internally monitor their own actions (BA24) or if they have deficits in self-perception, person perception or mentalizing (BA10). Being able to predict how parents will react, and being able to infer their parents' state of mind is probably quite adaptive. Hence, it is possible that the present findings were part of a preexisting constellation of neurobiological abnormalities that affected parent-child interactions and lead to an increased likelihood of exposure to CP or use of harsher disciplinary techniques. Prospective longitudinal studies will be required to untangle the nature of the relationship.

The present findings apply to HCP, which the AAP considers an unacceptable form of punishment. These findings do not necessarily generalize to milder, less frequent, and less persistent episodes of spanking that typically end before age 6, which the AAP considers an acceptable but not very effective form of discipline. How detrimental (or beneficial) spanking is depends on the age of the subject, frequency of administration, who administers the spanking, family context, and whether it is used as a primary means of discipline, or as a 'backup' strategy. However, the identification of neurobiological alterations in subjects exposed to HCP, and knowledge that CP is a risk factor for substance abuse, provides the impetus to ascertain whether there are correlates of exposure to ordinary episodes of CP.

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Figure 1.

Location and shape of regions of interest selected for analysis. Abbreviation: dorsolateral anterior cingulate cortex (dACC); dorsolateral prefrontal cortex (DLPFC); Nucleus Accumbens (NA); Substantia Nigra (SN); Globus pallidus (GP); Putamen (PUT); Caudate (CA); Thalamus (THA); Cerebellar Hemispheres (CBH).

Figure 2. Results of voxel-based relaxometry showing harsh corporal punishment > control differences in T2 relaxation time in right caudate and right putamen.

Table 1

Demographic characteristics, cognitive performance and symptom scores in controls and subjects exposed to harsh corporal punishment

Characteristics	Controls	Corporal Punishment	Statistics	
	N = 23	N = 19	(Anova, other)	p-value
Gender (Males/Females)	12M/11F	13M/6F	Fisher	0.35
Age (years)	22.0 ± 1.8	21.8 ± 2.4	0.06	0.81
Subject Education (years) ^a	14.4 ± 1.6	14.1 ± 1.5	0.51	0.48
Parental Education (years)	16.0 ± 2.4	14.4 ± 2.1	5.13	0.03
Perceived Financial Sufficiency	3.6 ± 0.7	3.1 ± 0.6	5.88	0.02
Drug use (days/month) ^{a,b}	0.7 ± 1.3	1.4 ± 5.1	0.41	0.53
Alcohol use (drinks/month)	12.8 ± 17.0	35.1 ± 65.3	2.38	0.13
Verbal IQ ^{a,b}	123.5 ± 15.0	117.7 ± 15.7	1.07	0.30
Performance IQ ^{a,b}	120.0 ± 12.2	116.3 ± 9.6	1.43	0.24
Full Scale IQ ^{a,b}	123.3 ± 14.3	118.8 ± 13.2	1.00	0.32
MAS Short-term memory ^{a,b}	113.2 ± 13.9	105.2 ± 11.2	3.68	0.06
MAS Verbal memory ^{a,b}	112.3 ± 15.5	109.0 ± 13.1	0.53	0.47
MAS Visual memory ^{a,b}	112.5 ± 9.2	109.0 ± 11.9	1.11	0.30
MAS Global memory ^{a,b}	114.5 ± 11.4	110.5 ± 11.3	1.31	0.26
SQ Anxiety ^{a,b}	3.75 ± 2.99	5.46 ± 3.73	2.56	0.12
SQ Depression ^{a,b}	2.29 ± 2.45	5.28 ± 4.59	6.92	0.01
SQ Somatization ^{a,b}	2.84 ± 2.52	4.25 ± 2.78	5.25	0.03
SQ Anger-hostility ^{a,b}	3.90 ± 3.19	4.81 ± 4.28	0.59	0.45

^a MAS - Memory Assessment Scale, SQ - Kellner Symptom Questionnaire Adjusted for age

^b MAS - Memory Assessment Scale, SQ - Kellner Symptom Questionnaire Adjusted for gender

Table 2

Partial correlations between memory performance measures and T2-RT in caudate and putamen.

	Caudate		Putamen	
	r	p-value	r	p-value
<i>All subjects</i>				
Short-term memory	-0.421	0.01	-0.332	0.05
Verbal memory	-0.358	0.03	-0.127	0.45
Visual memory	-0.440	0.006	-0.385	0.02
Global memory	-0.516	0.001	-0.314	0.06
<i>Controls</i>				
Short-term memory	-0.427	0.08	-0.024	0.92
Verbal memory	-0.132	0.60	0.323	0.19
Visual memory	-0.289	0.25	0.037	0.88
Global memory	-0.255	0.31	0.281	0.26
<i>Corporal Punishment</i>				
Short-term memory	-0.395	0.13	-0.542	0.03
Verbal memory	-0.586	0.02	-0.431	0.10
Visual memory	-0.524	0.04	-0.653	0.006
Global memory	-0.723	0.002	-0.709	0.002

Table 3
T2-relaxation time in regions of interest analyzed for differences between groups, hemispheres and interaction.

Regions of Interest	Control		Corporal Punishment		Statistical Differences (p-values)		
	Right	Left	Right	Left	Group	Hemisphere	Group × Hem
Anterior Cingulate Cortex	67.16 ± 2.39	67.56 ± 2.88	67.77 ± 2.31	69.51 ± 2.79	0.11	0.03	0.09
Caudate	61.08 ± 1.50	61.72 ± 2.19	62.49 ± 2.00	62.90 ± 1.88	0.02	0.74	0.58
Cerebellar Hemispheres	71.34 ± 1.39	71.28 ± 2.24	71.35 ± 1.46	71.02 ± 2.47	0.81	0.28	0.40
Dorsolateral Prefrontal Cortex	65.99 ± 1.55	66.21 ± 2.47	67.25 ± 2.80	67.71 ± 2.15	0.03	0.98	0.75
Globus Pallidus	52.26 ± 4.30	49.76 ± 4.02	53.19 ± 4.05	51.72 ± 4.20	0.21	0.13	0.35
Nucleus Accumbens	62.24 ± 1.83	66.34 ± 2.99	63.92 ± 2.16	66.30 ± 2.71	0.25	0.19	0.007
Putamen	56.79 ± 2.04	56.93 ± 2.26	58.59 ± 2.04	58.30 ± 2.36	0.01	0.10	0.003
Substantia Nigra	59.98 ± 2.72	62.01 ± 3.81	62.82 ± 3.13	62.81 ± 3.61	0.05	0.10	0.02
Thalamus	61.01 ± 1.83	61.49 ± 2.53	62.64 ± 1.75	62.87 ± 2.51	0.03	0.35	0.26

Table 4

Correlations for the relationship between regional T2-RT in dopamine-rich regions and extent of drug and alcohol use.

Region	Drug Use		Alcohol Use	
	r	p-value	r	p-value
Anterior Cingulate Cortex	0.406	0.009	0.392	0.012
Caudate	0.133	0.412	0.089	0.584
Dorsolateral Prefrontal Cortex	0.416	0.008	0.444	0.004
Nucleus Accumbens	-0.225	0.163	-0.204	0.206
Putamen	0.105	0.521	0.067	0.682
Substantia Nigra	0.140	0.390	0.038	0.814

Values in bold are significant with an overall False Discovery Rate < 0.05