Basal ganglia volumes following CO poisoning: A prospective longitudinal study.

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Pulsipher DT, Hopkins RO, Weaver LK. Basal ganglia volumes following CO poisoning: A prospective longitudinal study. UHM 2006; 33(4):245-256. Carbon monoxide (CO) poisoning may result in focal and diffuse neuropathological changes, including basal ganglia lesions. The effect of CO poisoning on basal ganglia volumes over time is unclear. We assessed basal ganglia volumes longitudinally following CO poisoning. We prospectively enrolled 73 CO poisoned patients who underwent brain MR imaging on day 1 (baseline), 2 weeks, and 6 months post-CO poisoning. Basal ganglia volumes were obtained. One patient had bilateral globus pallidus lesions at two weeks and 6 months. Of the CO-poisoned patients 28% had volume reduction in at least one basal ganglia structure by 6 months, of which 21% had putamen, 15% had caudate, 15% had globus pallidus, and 16% had total basal ganglia volume reduction. Putamen volumes were significantly smaller from baseline to six months (p = 0.02). Verbal memory and mental processing speed correlated with smaller putamen and globus pallidus volumes. Carbon monoxide poisoning results in basal ganglia volume reduction 6 months post CO poisoning. Slow mental processing speed and impaired memory correlated with smaller putamen and globus pallidus volumes. Clinicians need to be aware of basal ganglia neuropathologic changes in the absence of observable lesions following CO poisoning.

INTRODUCTION

Carbon monoxide (CO) poisoning is a significant health problem and is the major cause of poisoning deaths in the United States and Europe (1, 2). There are approximately 2000 to 6000 deaths and 40,000 emergency room visits in the United States each year from CO poisoning (3, 4). Carbon monoxide is a colorless, odorless gas produced as a by-product of combustion and common sources are internal combustion engines and faulty furnaces (5-7). Mechanisms of brain injury following CO poisoning include hypoxia (8, 9), lipid peroxidation resulting in oxidative injury (10), damage to the vascular endothelium due to deposition of peroxynitrate (11), inflammation (12), excitotoxicity (13), apoptosis or programmed cell death (14, 15), lactic acidosis (16), and inhibition of mitochondrial function (17).

Neuropathologic findings following CO poisoning include lesions of the basal ganglia (18), thalamus (19), substantia nigra (20), cortex, white matter, hippocampus, and cerebellum (1, 21-23). Generalized and focal atrophy of the corpus callosum (24), fornix (25), and hippocampus (1) occur following CO poisoning. Globus pallidus and white matter lesions are the most common neuropathologic findings (22, 26-28). The prevalence of basal ganglia lesions is heterogeneous and range from 8% to 78% (29, 30).
The primary function of the basal ganglia is to assist in the smooth coordination of motor movement (31). Basal ganglia lesions can affect cognitive and emotional function resulting in impaired concentration, confusion, irritability, and/or euphoria (31). The basal ganglia regulates voluntary movements involved in planning and initiating motor behavior and may also be important for some types of memory (32). The basal ganglia are also involved in the integration of internal motivation with behavior (33). Lesions of the putamen, caudate nucleus, globus pallidus, and internal capsule may cause aphasia, impair auditory comprehension and repetition, and disrupt the integration of sensory and motor output (34). Thus, CO-induced basal ganglia damage may contribute to the observed cognitive and neurological morbidity following CO poisoning.

While a number of studies have reported basal ganglia lesions following CO poisoning, there are no studies that have assessed basal ganglia volumes over time. The purpose of this study was to assess basal ganglia volumes at 2 weeks and 6 months compared to baseline (day 1) volumes in CO poisoned patients. The second purpose of this study was to assess the relationships between basal ganglia volumes and neuropsychological test scores.

**METHODS**

**Subjects**

Patients with acute CO poisoning were recruited from the Hyperbaric Medicine Service at LDS Hospital. There were 135 eligible CO poisoned patients, of whom 73 patients were enrolled and 62 patients declined the study. Reasons for study refusal include: not interested in study (N=21), cost of transport or treatment (N=17), inconvenience (N=14), not able to complete follow-up [i.e. out of state] (N=5), and the physician did not refer patient to the study (N=5). Patients were eligible if they had a documented exposure to CO measured by an elevated carboxyhemoglobin (COHb) level or elevated ambient CO concentration, or an obvious exposure to CO and symptoms of CO poisoning. Patients were excluded from the treatment study if they were more than 36 hours post-CO poisoning, if age < 16 years, moribund, informed consent was not obtained, or pregnant. Patient demographic and medical data including mode of CO poisoning, loss of consciousness (LOC) duration, COHb levels, laboratory data, and brain imaging data were collected prospectively. Using a prospective within-subjects design, 73 consecutive CO poisoned patients were enrolled in this study. This study had LDS Hospital Institutional Review Board approval and conformed to institutional and federal guidelines for the protection of human subjects. All patients signed statements of informed consent.

**Neuropsychological Tests**

The CO-poisoned patients were administered a neuropsychological test battery consisting of Digit Span, Digit Symbol and Block Design from Wechsler Adult Intelligence Scale-Revised (35), Trail Making Test Parts A and B (36), and Story Recall from the Denman Neuropsychology Memory Scale (37). The tests were administered on the day of CO poisoning (day 1), 2 weeks, and 6 months post-CO poisoning (4). Age, gender, and education corrected T-scores were used for data analysis (mean = 50, standard deviation = 10) (38, 39).

Cognitive sequelae were defined *a priori* and considered present if any 6-month neuropsychological subtest score was >2 standard deviations (SD) below the mean, or if 2 or more subtest scores were each >1 SD below the mean of demographically-corrected standardized T-scores (mean=50; SD=10). If the patient complained of memory, attention, or concentration difficulties, the required decreases in neuropsychological subtest scores were
>1 SD below the mean of demographically-corrected standardized T-scores on any one subtest (4).

**Imaging**

Enrolled patients were scanned within the first 24 to 36 hours (day 1 or baseline scan), at 2 weeks, and at 6 months following CO poisoning using a 1.5 Tesla quadrature head coil GE Signa Scanner (General Electric, Milwaukee, WI). All patients were imaged supine with the head in a fixed position, using the same scanner and protocol. Sagittal scans were T1-weighted, 500/11/2 (repetition time/echo time/excitations) with a 256 X 192 pixel acquisition matrix and a field of view (FOV) of 22 cm. Sagittal images were 5 mm thick with a 1 mm interspace gap. Axial intermediate and T2-weighted (3000/31; 90/1; repetition time/echo time excitations) spin echo images were acquired with slice thickness of 5 mm and 2 mm interspace gap, FOV of 22 cm, with acquisition matrix of 256 X 192. Coronal intermediate and T2-weighted (3800/21; 105/2) fast spin-echo images were acquired with 3 mm thick interleaved sections. A 22-cm FOV was used with a 512 X 256 acquisition matrix. The scan range extended from the most inferior point of the cerebellum to the most superior point of the cerebral cortex on the mid-sagittal image. Imaging data remained in digital form throughout the analysis.

**Volumetric Image Analysis**

The intermediate-weighted and T2-weighted images were processed and quantified as described in Blatter et al. (1995) using Analyze® (VCH Publishers, New York, New York) visualization and analysis software (40, 41). Image preparation, segmentation, and quantitative (volumetric) analyses were performed per the methods described previously (42). Briefly, regions of white matter, gray matter, and cerebrospinal fluid were identified and plotted to represent pixel signal intensity, which classifies the gray matter, white matter, and cerebral spinal fluid. Dual-echo intermediate-weighted and T2-weighted images are co-registered resulting in enhanced accurate signal identification. A multispectral segmentation was performed on the two spatially registered images (intermediate-weighted and T2-weighted) from the foramen magnum to the vertex (43). The quantitative MR image analysis results in volumetric rather than planimetric measures (i.e. cross-sectional surface area). The multispectral segmentation was performed for each individual scan (day 1, 6 months and 12 months) for each CO poisoned patient.

The scans were analyzed with the raters’ blind to patient identity, scan date, and neurocognitive outcome. The basal ganglia volumes were determined by using the region of interest feature of Analyze that yields a count of gray matter, white matter, and cerebral spinal fluid pixels. The segmentation step identifies the interface between cerebral spinal fluid and brain, and the trace feature was used to mark the boundaries of each structure (see below). The caudate were identified and traced in the coronal plane starting at the head of the caudate nucleus and proceeding posteriorly until the tail of the caudate was no longer visible. The boundaries for the head of the caudate were the anterior horn of the lateral ventricle and cortical white matter as lateral borders. For the putamen, the superior boundary was the lateral limb of the internal capsule and the inferior boundary was the anterior commissure or the pontes grisei caudatolenticulares. The lateral boundary for the putamen was the external capsule. For the globus pallidus, the pars medialis and pars lateralis were traced together with the internal capsule as the superior-medial border and the anterior commissure was the inferior boundary.

Caudate volumes were obtained by
summing the white and gray matter pixels and then multiplying by the voxel dimension. All structural volumes are the sum of both the gray and white matter, but are predominately gray matter. The same procedure was followed for the putamen and globus pallidus. The total basal ganglia volume was obtained by summing the volumes of the caudate, putamen, and globus pallidus volumes (Figure 1, see page 251). The above process was carried out for each CO-poisoned patient’s scans at day 1, 2 weeks, and 6 months. Structural volumes at baseline were obtained for the caudate, putamen, globus pallidus, and total basal ganglia by summing the volumes of the entire CO poisoned patients’ volumes and then calculating the mean and standard deviation for each structure.

Differences in head size were corrected using the total intracranial volume (TICV) by multiplying each volume by a ratio of the group mean TICV (1396 cm³) divided by each patients’ measured TICV. A priori the presence of volume reduction was defined as a decrease of $>1$ SD below the mean volumes of the CO patients’ baseline (day 1) scans for each structure (caudate, putamen, globus pallidus, and total basal ganglia). Thus, each patient served as their own control. Normal subjects have a 0.13% change in brain volume from baseline (initial scan) compared to scans done 6 months to 30 months later (43). Thus, our definition of $>1$ SD decline within 6 months is a conservative measure, well beyond the expected normal age related change.

Reliability
A single rater was trained under the direction of a neuroradiologist. A randomly selected group of 10 MR images was used for intrarater and interrater reliabilities. This group of images was analyzed at two separate times by the single rater to determine the intrarater reliability for all structures. Intrarater and interrater reliability exceeded 0.95 for all structures.

STATISTICAL ANALYSES
Using SPSS 13 (SPSS, Chicago, IL), descriptive statistics were calculated for demographic and medical data, and caudate, putamen, globus pallidus, and total basal ganglia volumes. Volumetric data are shown as mean ± standard deviation both for corrected and uncorrected volumes. Because uncorrected volumes were not significantly different from corrected volumes, all analyses were conducted using the uncorrected volumes unless otherwise specified.

A repeated measures analysis of variance (RMANOVA) compared caudate, putamen, globus pallidus, and total basal ganglia volumes over time (day 1, 2 weeks, and 6 months). A Mann-Whitney U test compared patients with volume reduction to patients with no volume reduction for age, sex, education, suicide, LOC duration, and COHb. A chi-square compared patients with volume reduction to patients with no volume reduction for sex and suicide.

Correlations assessed relationships between individual CO poisoning variables and basal ganglia volumes. Point biserial correlations were used for categorical variables (e.g. sex, loss of consciousness, duration of LOC, and suicide-attempt), and Pearson’s correlations were used for continuous variables (e.g. age, COHb level, and education). The variables included in the correlation analyses were selected a priori by consensus based on clinical relevance, as the variables have been reported to be related to poor neurologic and cognitive outcomes following CO poisoning or have known effects on brain volumes (e.g. age).

Pearson’s and point biserial correlations assessed the relationships between basal ganglia volumes and cognitive sequelae (presence or absence) at 2 weeks and 6 months, and
between basal ganglia volumes and individual neuropsychological test scores.

RESULTS

There were 73 CO poisoned patients, 49 males and 24 females, with a mean age of 34.9 ± 13.6 years (range 16 to 86 years), and mean education level of 12.3 ± 2.5 years (range 2 to 20 years). The CO patients’ mean COHb level was 21.7 ± 10.9% (range 0 to 39%). Fifty-four percent (n=39) of the patients had loss of consciousness. The mode of CO poisoning was accidental for 77% (n=56) of patients and 22% (n=16) were suicide-attempt. At 6 months, 35.6% of the patients had cognitive sequelae.

The corrected and uncorrected volumes for the basal ganglia structures at all 3 follow-up times are shown in Table 1 (see page 250). At two weeks 20.5% (15/73) and at 6 months 28.8% (21/73) of the CO poisoned patients had volume reduction in at least one structure. Figure 2 (see page 252) shows the percent of patients with volume reduction for the caudate, putamen, globus pallidus and total basal ganglia at 2 weeks and 6 months. All patients with volume reduction at 2 weeks had volume reduction at 6 months with additional volume loss at 6 months suggesting progressive volume loss over time.

There were 6 patients with no volume reduction at 2 weeks, who had volume reduction at 6 months. Eleven percent (8/73) of CO poisoned patients had volume reduction in one structure, 12.3% (9/73) in two structures, and 5.5% (4/73) had volume reduction in all three structures at 6 months. Between day 1 and 6 months the mean volume change for the caudate was -1.3% (range 0.44% to -3.6%), putamen - 3.4% (range 3.7% to -12.5%), globus pallidus 2.6% (range 2.6% to -10%), and total basal ganglia of 2.4% (range 2% to -7.9%). Only one patient had basal ganglia lesions that were present at 2 weeks and 6 months, suggesting that lesions did not account for the observed volume reductions.

Repeated measures analysis of variance (RMANOVA) showed significant volume reduction for the uncorrected putamen (F = 3.86, p = 0.027; partial η² = 0.051) and corrected putamen (F = 4.38, p = 0.018; partial η² = 0.057). There were consistently small but non-significant volume reductions for corrected and uncorrected volumes for the caudate, globus pallidus, and total basal ganglia. However, there was a trend for the corrected total basal ganglia volume reduction (F = 2.87, p = 0.06; partial η² = 0.038). Effect sizes using partial eta squared (partial η²) for the uncorrected caudate, globus pallidus, and total basal ganglia were 0.025, 0.012, and 0.035, respectively.

Table 2

Table 2 (see page 250) shows comparisons for demographic and CO poisoning variables for patients with basal ganglia volume reduction compared to those with no volume reduction. A Mann-Whitney U test for patients with any structural volume reduction >1 SD (mean age 44 ± 17.1 years) compared to those with no volume reduction ≤1 SD (mean age 31.2 ± 9.9 years) at 6 months found that older patients (Mann-Whitney U = 282.5, p = 0.001) and longer LOC duration (Mann-Whitney U = 346.5, p = 0.013) resulted in greater volume reduction. However, there were no volume differences for sex (χ² = 1.331, p = 0.25) or suicide-attempt (χ² = 2.646, p = 0.11).

At 6 months, older age correlated with caudate (r = -0.408, p < 0.001), putamen (r = -0.323, p = 0.005), and total basal ganglia volumes (r = -0.386, p = 0.001). Suicide-attempt correlated with caudate (r = 0.254, p = 0.030), putamen (r = 0.285, p = 0.015), and total basal ganglia volumes (r = 0.289, p = 0.013). Female sex (r = 0.318, p = 0.006) and higher COHb levels (r = 0.236, p = 0.044) correlated with putamen volumes. Loss of consciousness and CO
### Table 1. Basal ganglia volumes

<table>
<thead>
<tr>
<th>Volumes (cm³)</th>
<th>Uncorrected Mean ± SD</th>
<th>Corrected for TICV Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Day of CO Poisoning</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caudate</td>
<td>7.85 ± 1.21</td>
<td>7.90 ± 1.25</td>
</tr>
<tr>
<td>Putamen</td>
<td>8.85 ± 0.86</td>
<td>8.93 ± 1.05</td>
</tr>
<tr>
<td>Globus Pallidus</td>
<td>2.33 ± 0.42</td>
<td>2.34 ± 0.40</td>
</tr>
<tr>
<td>Total Basal Ganglia</td>
<td>19.03 ± 2.21</td>
<td>19.17 ± 2.41</td>
</tr>
<tr>
<td><strong>2 weeks post-CO Poisoning</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caudate</td>
<td>7.92 ± 1.28</td>
<td>7.92 ± 1.17</td>
</tr>
<tr>
<td>Putamen</td>
<td>8.72 ± 1.50</td>
<td>8.72 ± 1.37</td>
</tr>
<tr>
<td>Globus Pallidus</td>
<td>2.34 ± 0.51</td>
<td>2.34 ± 0.47</td>
</tr>
<tr>
<td>Total Basal Ganglia</td>
<td>18.99 ± 2.92</td>
<td>18.99 ± 2.66</td>
</tr>
<tr>
<td><strong>6 months post-CO Poisoning</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caudate</td>
<td>7.75 ± 1.35</td>
<td>7.78 ± 1.16</td>
</tr>
<tr>
<td>Putamen</td>
<td>8.55 ± 1.52*</td>
<td>8.57 ± 1.43*</td>
</tr>
<tr>
<td>Globus Pallidus</td>
<td>2.27 ± 0.55</td>
<td>2.27 ± 0.50</td>
</tr>
<tr>
<td>Total Basal Ganglia</td>
<td>18.58 ± 3.09</td>
<td>18.63 ± 2.72</td>
</tr>
</tbody>
</table>

Table 1. Uncorrected and corrected volumes in cm³ are shown for the caudate, putamen, globus pallidus, and total basal ganglia. Data are presented as mean ± standard deviation. * Indicates a significant difference between Day of CO poisoning and 6 months (p < 0.03). Abbreviations are as follows: CO = Carbon monoxide, SD = standard deviation, TICV = total intracranial volume.

<table>
<thead>
<tr>
<th></th>
<th>U</th>
<th>z</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>469.5</td>
<td>-1.15</td>
<td>0.25</td>
</tr>
<tr>
<td>Age</td>
<td>282.5</td>
<td>-3.21</td>
<td>0.001</td>
</tr>
<tr>
<td>Education</td>
<td>508</td>
<td>-2.18</td>
<td>0.83</td>
</tr>
<tr>
<td>Suicide</td>
<td>451</td>
<td>-1.16</td>
<td>0.11</td>
</tr>
<tr>
<td>LOC duration</td>
<td>346</td>
<td>-2.49</td>
<td>0.01</td>
</tr>
<tr>
<td>COHb</td>
<td>498.5</td>
<td>-0.58</td>
<td>0.56</td>
</tr>
</tbody>
</table>

Table 2. Mann-Whitney U test comparing CO poisoned patients with basal ganglia atrophy at 6 months compared to patients with no atrophic changes at 6 months.
Fig. 1. Coronal magnetic resonance imaging through the basal ganglia.

Fig 1. Figure 1 shows a T1 weighted coronal image through the basal ganglia. The caudate is shown with the letter A, putamen with the letter B, and the globus pallidus with the letter C. The black outlines show the boundaries of the basal ganglia structures.
exposure duration did not correlate with any structural volume.

There were no significant correlations between basal ganglia volumes and cognitive sequelae (presence or absence) at 2 weeks or 6 months. Although the presence of cognitive sequelae did not correlate with basal ganglia volumes, there was a significant relationship between basal ganglia volumes and two individual neuropsychological test scores: Digit Symbol (mental processing speed) correlated with caudate ($r = .235, p = .05$), putamen ($r = .300, p = .01$), globus pallidus ($r = .265, p = .02$), and total basal ganglia ($r = .305, p = .009$) volumes at two weeks. Digit Symbol correlated with the putamen ($r = .246, p = .04$), globus pallidus ($r = .256, p = .03$), and total basal ganglia ($r = .247, p = .04$) volumes at 6 months. Story Recall (verbal memory) correlated with putamen ($r = .238, p = .047$), globus pallidus ($r = .247, p = .04$) and total basal ganglia ($r = .251, p = .04$) volumes at 6 months. The correlations were in the expected direction with smaller volumes correlating with lower neuropsychological scores.

**DISCUSSION**

Twenty-one percent of our CO-poisoned patients had volume reductions in the putamen, 15% caudate, 15% globus pallidus, and 16% for the total basal ganglia. Between 1 day and 6 months the mean volume change for the caudate was -1.3%, putamen - 3.4%, globus pallidus 2.6%, and total basal ganglia of 2.4%. Normal
healthy subjects have a 0.13% decline in brain volume on serial scans 6 months to 30 months apart (43). Therefore the volume reduction in our CO-poisoned patients is greater than what would be expected due to normal aging.

Only one subject had basal ganglia lesions at 2 weeks and 6 months (1, 21-23), compared to 16% with total basal ganglia volume reduction at 6 months. Support for the observed basal ganglia damage (i.e. volume reduction) comes from studies of basal ganglia lesions in CO-poisoned patients. Studies show variable prevalence rates in basal ganglia lesions from 7.8% (44), 25.6% (45), 42.5% (46), to 63.3% (2), suggesting that the basal ganglia is vulnerable to CO-induced injury. While bilateral lesions of the globus pallidus occur following CO poisoning (22, 26-28, 47, 48), only one patient in our group had basal ganglia lesions suggesting that the observed basal ganglia volume reduction was not due to observable necrosis.

Lesions of the caudate and putamen following CO poisoning occur less frequently than globus pallidus lesions (49, 50). Previous research indicates that 4% of CO-poisoned patients have lesions in the caudate, 5% putamen, and 29% globus pallidus lesions (51). However, 15% of our CO poisoned patients had caudate volume reduction that did not reach significance in the multivariable analysis, whereas 21% had putamen volume reduction that was significant. The above findings suggest that while globus pallidus lesions may be more common than caudate or putamen lesions following CO poisoning, more patients had volume reduction in the putamen compared to the caudate or globus pallidus. The magnitude of the volume reduction was comparable for all three structures. Our data suggest that CO poisoning may result in volume reduction in the absence of observable lesions.

Older age and suicide-attempt correlated with caudate, putamen and total basal ganglia volumes. Higher COHb levels and female sex correlated with putamen volumes. However there were no correlations with globus pallidus volumes. The lack of correlation with globus pallidus volumes is surprising since globus pallidus lesions are common following CO poisoning (22, 26-28, 47, 48). The above findings are interesting in light of data that show that markers of CO poisoning severity such as COHb levels are not related to initial symptoms, neurologic or cognitive sequelae (44, 52-59). Whereas, we found that higher COHb levels were associated with putamen volume reduction.

The patients with significant volume reduction (>1 SD) were compared to those with no volume reduction at 6 months. Although LOC did not correlate with volumes for the entire group, we found that older patients with a longer LOC duration had the greatest basal ganglia volume reduction compared to CO poisoned patients with no volume reduction. Striatal nuclei volumes decrease in older health adults, suggesting that basal ganglia volume reduction may occur due to normal aging (60). While Raz and colleagues found a linear relationship in basal ganglia volume reduction with increasing age, it is unlikely that the volume reductions in our study were due to normal aging. First, the mean age of our CO-poisoned patients was 34 years, which is significantly younger than the subjects in the Raz et al., study (mean age of 57 years). Second, the volume reductions observed in our CO-poisoned patients occurred over a brief 6-month period, while in Raz et al.’s study basal ganglia volumes were assessed over five years. It is unlikely that basal ganglia volumes would significantly decline in healthy adults in such a brief period of time as observed in our CO-poisoned patients. Thus, the observed basal ganglia volume reductions in our CO-poisoned patients are more likely due to the effects of CO poisoning rather than ageing.
We found slow mental processing speed and impaired memory correlated with smaller putamen and globus pallidus volumes. Similar to our findings, basal ganglia lesions are associated with impaired learning, memory (61), and attention (62). Alternatively, impaired verbal memory associated with fornix atrophy (25) and slow mental processing speed associated with white matter hyperintensities (23) were reported in the same group of CO poisoned patients used in the current study. Thus, basal ganglia volume reduction plus fornix atrophy and white matter hyperintensities likely all contribute to the observed cognitive impairments in CO poisoned patients. The presence or absence of cognitive sequelae did not correlate with basal ganglia volumes. However measures of memory and mental processing speed were related to basal ganglia volume reduction, suggesting the observed volume reduction in our patients contributed to their cognitive impairments.

There are several strengths of this study, including the quantitative MR analysis in a prospective within-subjects repeated measures design that provided baseline brain scans, enabling us to detect subtle basal ganglia volume reduction that may have otherwise been missed. Because brain volume loss is unlikely to occur within 24 hours after poisoning, the CO poisoned patients' initial MR brain scans are good indicators of their premorbid brain morphology, which can be used as a baseline for comparison with subsequent scans. In addition, the basal ganglia volumes were measured using a standardized protocol. Finally, selection bias was minimized because we enrolled CO-poisoned patients with a range of poisoning severity, not just individuals with severe CO poisoning or those with lesions in the basal ganglia.

There are several limitations of the study, including the lack of tests of motor function in our neuropsychological test battery. We selected our neuropsychological tests for their known sensitivity to the neurocognitive deficits observed following CO poisoning (4, 56), including impaired attention, memory, executive function and mental processing speed. Due to the small effect sizes, a larger prospective study is needed to replicate our findings. Future research should assess the contribution of the basal ganglia volume reduction on functional outcomes such as motor function and reward-based learning in a larger group of patients.

Carbon monoxide results in caudate, putamen and globus pallidus volume reduction 6 months post-CO poisoning. Older age and suicide attempt were associated with smaller caudate, putamen, and total basal ganglia volumes and higher COHb levels and female sex were associated with smaller putamen volumes. Slow mental processing speed and impaired memory correlated with smaller putamen and globus pallidus volumes. Clinicians and researchers need to be aware of neuropathologic changes following CO poisoning and remain vigilant about CO prevention.

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