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Longitudinal Brain Perfusion Findings in a Patient With Cognitive Symptoms and a History of Mercury Exposure: A Case Report

Binh Pham [1, 2, 3]

1. Psychiatry, Western University of Health Sciences, Pomona, USA 2. Sleep Medicine, Amen Clinics, Costa Mesa, USA 3. Sleep Medicine, Southwest Healthcare Medical Education Consortium, Temecula, USA

Corresponding author: Binh Pham, bpham@completesleepsolutions.com

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Abstract

A 42-year-old man presented with persistent brain fog, intermittent word-finding difficulty, reduced concentration, and decreased work efficiency in the setting of prior dental amalgam exposure. Baseline urinary mercury obtained without chelator provocation was below the analytical limit of detection, whereas a later post-2,3-dimercapto-1-propanesulfonic acid (DMPS) specimen showed increased urinary mercury excretion that was not interpreted as evidence of mercury toxicity or as a quantitative measure of mercury burden. Brain perfusion single-photon emission computed tomography (SPECT) performed under resting and concentration conditions showed multiple qualitative regional differences in relative tracer distribution. Repeat resting SPECT approximately eight months later was interpreted as showing less pronounced relative decreases in several cortical regions, while other regional differences persisted. The patient subsequently reported modest subjective improvement, although cognitive symptoms remained variable. This case provides a longitudinal description of qualitative brain perfusion findings but does not establish that prior dental amalgam exposure caused the patient's symptoms, that the SPECT findings represented mercury neurotoxicity, or that interval imaging differences reflected treatment response. Brain perfusion SPECT should therefore be interpreted as an adjunctive descriptive modality within the broader clinical, toxicological, and neurological assessment.

Categories: Nuclear Medicine, Environmental Health, Neurology
Keywords: brain perfusion spect, case report, cerebral perfusion, chelation, cognitive symptoms, dental amalgam, dmps, functional neuroimaging, mercury exposure, neurotoxicity

Introduction

Mercury exposure has long been associated with neurological and neurobehavioral effects, although the clinical manifestations vary according to the chemical form of mercury, route and magnitude of exposure, and duration of exposure [1,2]. Reported effects of clinically significant elemental mercury exposure in adults include tremor, impaired motor coordination, changes in mood and behavior, and reduced cognitive performance involving domains such as attention, memory, and psychomotor function [2]. A remote history of dental amalgam exposure, however, does not by itself establish mercury toxicity or mercury-related neurological disease. In the present case, post-chelation urinary mercury testing is likewise interpreted cautiously and is not treated as a validated measure of total-body mercury burden or diagnostic evidence of toxicity. Because these manifestations and exposure histories are heterogeneous and often nonspecific, establishing an individual causal relationship between remote exposure and persistent cognitive symptoms can be difficult.

Brain perfusion single-photon emission computed tomography (SPECT) is a functional imaging technique that uses technetium-99m-labeled radiopharmaceuticals to depict relative regional tracer uptake as an indirect representation of cerebral perfusion [3]. In contrast to structural magnetic resonance imaging, which primarily depicts brain anatomy, perfusion SPECT characterizes relative patterns of regional perfusion. These patterns are nonspecific and may overlap across neurological, psychiatric, metabolic, and toxic conditions. Accordingly, particularly in patients with nonspecific cognitive complaints, brain perfusion SPECT cannot independently establish a diagnosis or etiology and should be interpreted only in conjunction with the clinical history, examination, laboratory findings, and conventional diagnostic studies [3].

Published brain perfusion SPECT observations in mercury exposure remain sparse. O'Carroll et al. reported abnormal posterior cingulate SPECT activity in a patient with prior toxic inorganic mercury exposure despite an unremarkable structural magnetic resonance imaging study [4]. Rhee et al. subsequently described cerebellar perfusion defects in a patient with mercury vapor intoxication and cerebellar ataxia [5]. These isolated reports are heterogeneous and do not establish a reproducible mercury-specific perfusion pattern or clarify how qualitative perfusion findings may change longitudinally. We present a 42-year-old man with persistent cognitive symptoms and a remote history of mercury-containing dental amalgam exposure who underwent resting and concentration brain perfusion SPECT followed by repeat resting imaging approximately eight months later. This case adds a longitudinal description of qualitative perfusion findings

while illustrating the interpretive limitations of remote exposure history, post-chelation urinary mercury testing, and nonspecific SPECT findings. The purpose of this report is descriptive: to characterize the longitudinal imaging findings while emphasizing that neither the initial findings nor their interval changes establish mercury-related neurotoxicity, clinical recovery, or treatment response.

Case Presentation

For deidentification, the initial clinical evaluation is designated Day 1, and subsequent events are reported relative to that evaluation rather than by calendar date.

A 42-year-old man presented on Day 1 for evaluation of persistent mild cognitive concerns characterized by brain fog, intermittent word-finding difficulty, occasional repetition of questions, and reduced efficiency with work-related tasks. The exact onset and duration of these cognitive symptoms before Day 1 could not be established from the records available for retrospective review. He reported a history of dental amalgam restorations beginning in childhood, with removal approximately four years before presentation, and expressed concern regarding possible long-term effects of mercury exposure on cognitive functioning. His medical history was also notable for Epstein-Barr virus infection approximately one year before presentation, followed by intermittent fatigue that had gradually improved but remained more noticeable with stress or exertion. He remained functionally independent and reported generally restorative sleep of seven to eight hours nightly. Family history was notable for Alzheimer disease in a first-degree relative. He denied a history of concussion, loss of consciousness, whiplash, other head trauma, substance misuse, or prior psychiatric or neurological treatment.

Baseline symptom assessment demonstrated a Patient Health Questionnaire-9 (PHQ-9) score of 4, consistent with minimal depressive symptoms. Computerized testing of attention, vigilance, and impulse control showed no atypical T-scores and did not suggest an attention-deficit disorder. Laboratory evaluation did not identify a clear major metabolic, endocrine, renal, hepatic, or nutritional explanation for the cognitive complaints. Hematocrit was mildly elevated at 51.9%, and vitamin B12 was above the laboratory reference interval at >2000 pg/mL. Laboratory findings most relevant to the cognitive evaluation and mercury assessment are summarized in Table *1*.

Timing relative to Day 1	Laboratory test	Result	Reference interval
Approximately eight months before Day 1	Urine mercury	Below LOD	<0.3 µg/g creatinine
Initial evaluation period	Hematocrit	51.90%	37.5–51.0%
	Glucose	90 mg/dL	70–99 mg/dL
	Creatinine	1.23 mg/dL	0.76–1.27 mg/dL
	eGFR	75 mL/min/1.73 m²	>59 mL/min/1.73 m²
	AST	15 IU/L	0–40 IU/L
	ALT	19 IU/L	0–44 IU/L
	HbA1c	5.00%	4.8–5.6%
	TSH	1.930 µIU/mL	0.450–4.500 µIU/mL
	Free T4	1.39 ng/dL	0.82–1.77 ng/dL
	Vitamin B12	>2000 pg/mL	232–1245 pg/mL
	Folate	16.1 ng/mL	>3.0 ng/mL
	Vitamin D, 25-hydroxy	38.4 ng/mL	30.0–100.0 ng/mL
	Ferritin	234 ng/mL	30–400 ng/mL
	hsCRP	0.56 mg/L	0.00–3.00 mg/L
	Homocysteine	7.4 µmol/L	0.0–14.5 µmol/L
Approximately three months after Day 1	Urine mercury after DMPS	207 µg/g creatinine	<1.3 µg/g creatinine
	Urine creatinine	0.33 g/L	0.40–2.78 g/L

TABLE 1: Selected laboratory findings relevant to the cognitive and mercury evaluation

The unprovoked urinary mercury result obtained before the initial evaluation was below the analytical limit of detection (LOD). Where the German laboratory report used the abbreviation “NWG” (Nachweisgrenze), this was translated as LOD for consistency. The later urine specimen was obtained following administration of 2,3-dimercapto-1-propanesulfonic acid (DMPS). The laboratory specified that its listed reference intervals applied to basal urine and that only approximate guidance values were available following chelation. Therefore, the post-DMPS mercury concentration should not be directly compared with the basal urine reference interval or interpreted as a validated measure of total-body mercury burden.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; DMPS, 2,3-dimercapto-1-propanesulfonic acid; eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; hsCRP, high-sensitivity C-reactive protein; LOD, limit of detection; NWG, Nachweisgrenze; T4, thyroxine; TSH, thyroid-stimulating hormone

The unprovoked urinary mercury specimen obtained approximately eight months before Day 1 was reported by the laboratory as below the analytical limit of detection. Approximately three months after Day 1, repeat urinary heavy-metal testing following DMPS administration yielded a urinary mercury concentration of 207 µg/g creatinine and a urine creatinine concentration of 0.33 g/L, below the laboratory reference interval of 0.40-2.78 g/L and consistent with a relatively dilute specimen. The laboratory specified that its reference intervals applied to basal urine and that only approximate guidance values were available following chelation. Accordingly, the post-DMPS result was not considered directly comparable with the earlier unprovoked result or a validated quantitative measure of total-body mercury burden.

Overall, the working clinical formulation was persistent cognitive symptoms of uncertain etiology rather than a mercury-related neurological syndrome. The cognitive complaints were primarily subjective, and a comprehensive formal neuropsychological battery was not performed; formal cognitive assessment was limited to computerized attention testing. Detailed neurological examination findings and a structural brain MRI report were not available among the records reviewed for this case. Potential contributors considered across the clinical course included residual post-viral fatigue, stress, sleep disruption, and frequent travel. Accordingly, the presentation is intended to document an individual longitudinal clinical course rather than define a distinct or reproducible mercury-related clinical phenotype.

The initial concentration SPECT study was obtained 13 days before Day 1, and the initial resting SPECT study was obtained 12 days before Day 1. Brain perfusion SPECT acquisition followed the clinic’s standard

imaging protocol. After administration of technetium-99m hexamethylpropyleneamine oxime (99mTc-HMPAO), tomographic images were obtained approximately 30 to 60 minutes later with a high-resolution gamma camera equipped with fan-beam collimation. A total of 120 projections were acquired over 360° at 3° increments using a 128 × 128 matrix. The reconstructed dataset incorporated low-pass filtering and linear attenuation correction and was reviewed in coronal, sagittal, and transaxial planes with an approximate reconstructed slice thickness of 9 mm. Three-dimensional surface renderings were additionally generated using a standardized linear display scale. These displays included surface maps representing the most active 45% of cerebral activity and complementary maps comparing mean activity with the most active 15%. Because complete patient-specific acquisition records were unavailable for retrospective review, the exact administered radiotracer activity, individual camera model and manufacturer, radiopharmaceutical manufacturer, numerical display-scale settings, and validated quantitative regional thresholds could not be independently confirmed.

The regional findings were derived from the qualitative interpretation documented in the clinical SPECT report rather than from validated quantitative regional analysis or a documented normative database comparison available for retrospective review. Both the resting and concentration studies were described as having overall decreased relative tracer activity, focal bilateral thalamic increases, and relatively decreased bilateral basal ganglia activity. Relative decreases involving the bilateral inferior orbitofrontal and temporal regions were described on both studies and as more pronounced at rest. Bilateral lateral and anterior prefrontal decreases were also described on both studies and as more pronounced during concentration. Bilateral parietal decreases were present on both studies. Occipital decreases were bilateral, with the right-sided decrease described as more pronounced at rest. Internal cerebellar decreases were also described on both studies. The clinical interpretation further described a greater number of focal cortical decreases during the concentration condition. Representative resting and concentration surface-rendered brain perfusion SPECT images are shown in Figure *1* and Figure *2*, respectively.

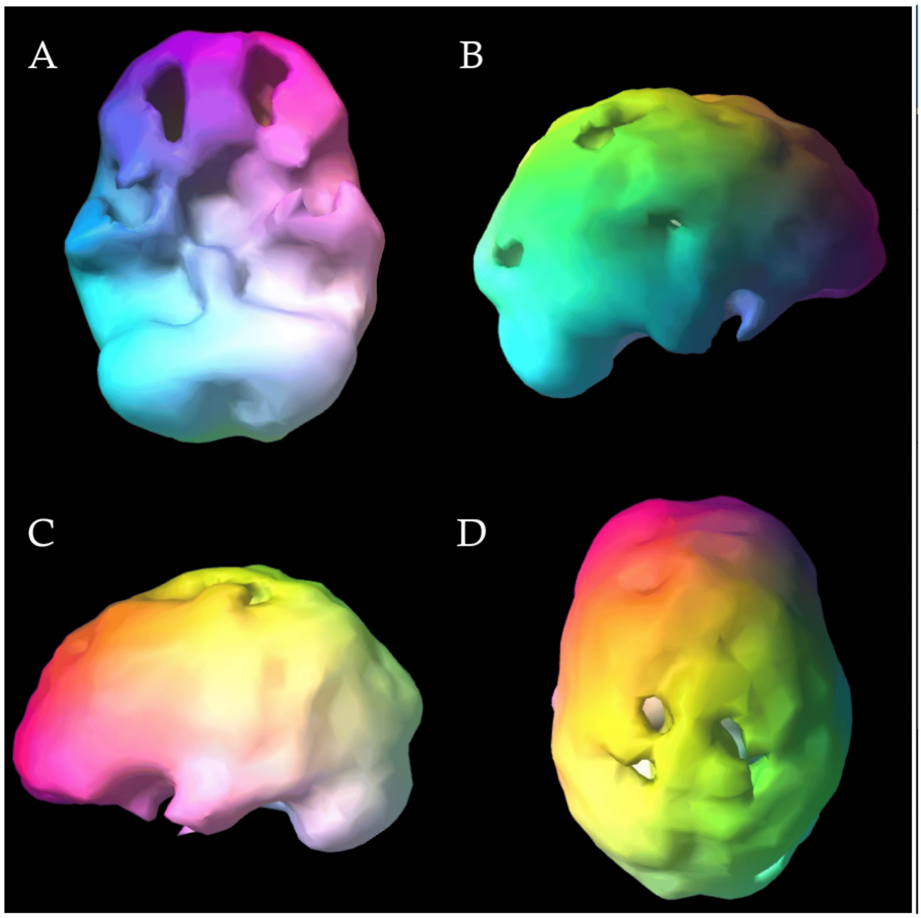


FIGURE 1: Resting surface-rendered brain perfusion SPECT images

Resting surface-rendered brain perfusion SPECT images showing the relative regional distribution of tracer activity. Warmer colors represent relatively greater tracer activity, whereas cooler colors represent relatively lower tracer activity within the reconstructed brain surface. (A) Inferior (underside) view. (B) Right lateral view. (C) Left lateral view. (D) Superior (top-down) view. According to the qualitative clinical interpretation, relative decreases were described involving the bilateral inferior orbitofrontal, temporal, prefrontal, parietal, occipital, and internal cerebellar regions, with relative decreases in the basal ganglia and focal bilateral increases in the thalami. The color-rendered images represent relative within-patient tracer intensity and do not provide direct absolute measurements of cerebral blood flow. A quantitative scale, validated regional thresholds, normative comparator map, and corresponding quantitative outputs were not available for retrospective inclusion. Accordingly, these images are presented for descriptive and illustrative purposes and are not independently diagnostic.

SPECT: single-photon emission computed tomography

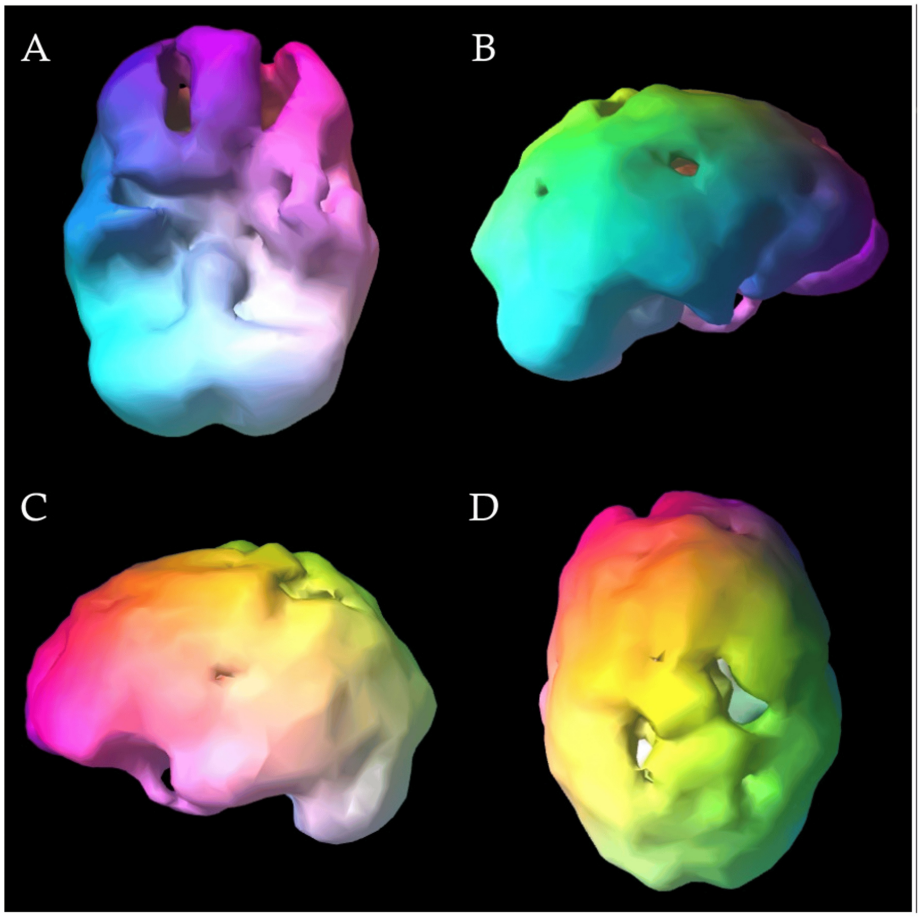


FIGURE 2: Concentration surface-rendered brain perfusion SPECT images obtained during the Conners Continuous Performance Test

Concentration surface-rendered brain perfusion SPECT images obtained during the Conners Continuous Performance Test and showing the relative regional distribution of tracer activity during sustained attentional demand. Warmer colors represent relatively greater tracer activity, whereas cooler colors represent relatively lower tracer activity within the reconstructed brain surface. (A) Inferior (underside) view. (B) Right lateral view. (C) Left lateral view. (D) Superior (top-down) view. According to the qualitative clinical interpretation, relative decreases were described involving the basal ganglia, inferior orbitofrontal, temporal, prefrontal, parietal, occipital, and internal cerebellar regions, with focal bilateral increases in the thalami. The lateral and anterior prefrontal decreases and the number of focal cortical decreases were described as more pronounced during the concentration condition. These findings represent relative regional tracer distribution and should not be interpreted as quantitative measurements of cerebral activation or absolute cerebral blood flow. The images are presented for descriptive and illustrative purposes and are not independently diagnostic.

SPECT: single-photon emission computed tomography

A specific etiologic diagnosis linking the cognitive symptoms to mercury exposure was not established. The working clinical formulation remained persistent cognitive symptoms of uncertain etiology in the context of remote mercury-containing dental amalgam exposure, a history of post-viral fatigue, and variable sleep- and stress-related factors. The post-DMPS urinary mercury result was treated as contextual information rather than as diagnostic evidence of mercury toxicity. The SPECT findings were likewise interpreted as adjunctive and nonspecific rather than as a diagnostic imaging pattern.

Management during the interval of observation was conservative and included lifestyle-oriented measures and nonprescription supplements. By clinical follow-up shortly before the Day 234 repeat SPECT study, the patient reported use of omega-3 fatty acids, vitamin D with vitamin K2, and N-acetylcysteine; the exact initiation dates of these supplements were not documented. No psychotropic medication was being used. Mercury chelation and plasmapheresis had been proposed by an outside clinician, but neither had been initiated before the repeat SPECT study.

At the clinical follow-up shortly before repeat imaging, approximately eight months after the initial evaluation, the patient reported that brain fog, concentration difficulty, word-finding problems, and work-related cognitive inefficiency were largely unchanged. Morning fatigue remained more noticeable than

evening fatigue. Frequent international travel and long flights intermittently disrupted sleep and routine, with associated fluctuations in fatigue and cognitive symptoms. Mood was generally stable, although he described episodic nervousness, worry, and transient low mood in the setting of stress. He denied suicidal ideation, homicidal ideation, hallucinations, or other acute psychiatric symptoms.

Repeat brain SPECT imaging was subsequently obtained under resting conditions on Day 234, approximately eight months after the initial resting study. A concentration acquisition was not performed; therefore, longitudinal comparison was limited to the resting studies. According to the qualitative clinical interpretation, relative decreases involving the inferior orbitofrontal, temporal, and frontoparietal regions remained present at follow-up but were described as less pronounced than on the initial resting study. Bilateral occipital decreases also remained present, with the left-sided decrease described as more pronounced and the right-sided decrease as less prominent than previously. Relative left basal ganglia activity remained decreased, whereas the previously described right basal ganglia decrease was no longer noted. Bilateral thalamic increases persisted, with greater relative prominence on the right at follow-up. Decreased internal cerebellar activity also remained present. These longitudinal differences reflected the qualitative clinical interpretation and were not based on validated quantitative between-session analysis. Representative surface-rendered images from the follow-up resting study are shown in Figure *3*; the corresponding initial resting images are shown in Figure *1* for longitudinal reference. Because the examinations were not quantitatively coregistered or standardized for direct image-to-image comparison, the figures are presented separately and should be interpreted descriptively.

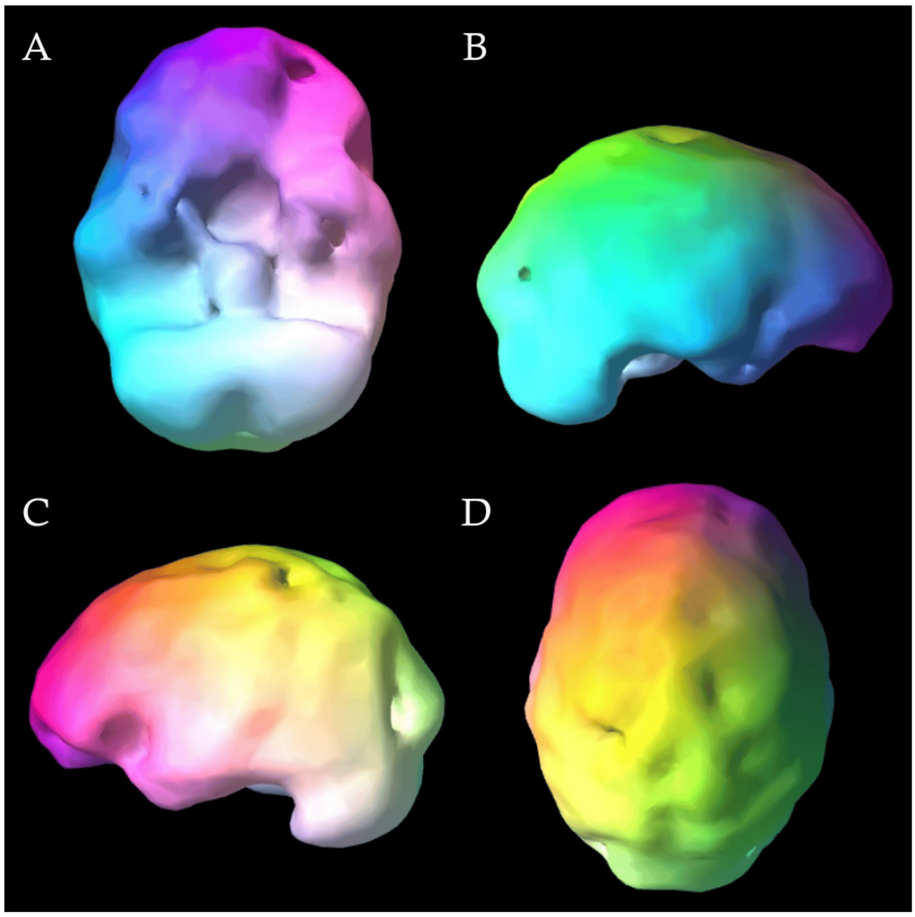


FIGURE 3: Follow-up resting surface-rendered brain perfusion SPECT images

Follow-up resting surface-rendered brain perfusion SPECT images showing relative regional tracer distribution. (A) Inferior view; (B) right lateral view; (C) left lateral view; (D) superior view. Compared qualitatively with the initial resting study shown in Figure 1, relative decreases involving the inferior orbitofrontal, temporal, and frontoparietal regions remained present but were described as less pronounced. Bilateral thalamic increases persisted, while regional differences involving the occipital regions, left basal ganglia, and internal cerebellar regions also remained present. The longitudinal comparison is descriptive and was not based on validated quantitative between-session analysis.

SPECT: single-photon emission computed tomography

At the subsequent follow-up approximately one month after repeat imaging, the patient reported modest overall improvement compared with his prior baseline, although symptoms remained variable. Mood was described as somewhat improved but continued to fluctuate, particularly during periods of frequent travel and occupational stress. Cognitive complaints, including brain fog and reduced concentration, persisted but varied in severity and were more noticeable with sleep disruption, fatigue, and increased workload. He continued omega-3 fatty acids, vitamin D with vitamin K2, and N-acetylcysteine, which had been documented before the repeat SPECT study. At this follow-up, he also reported use of a saffron-containing supplement and a cognitive-support supplement without a clear subjective cognitive benefit. He was not taking psychotropic medication. He additionally reported use of an infrared photobiomodulation device, which he subjectively associated with some improvement. The initiation dates of the saffron-containing supplement, cognitive-support supplement, and photobiomodulation device were not documented; therefore, whether these interventions began before or after the Day 234 repeat SPECT study could not be established. Overall, the clinical course was characterized by partial subjective improvement with persistent fluctuating cognitive symptoms during the period in which qualitative interval differences were observed on resting SPECT imaging.

Discussion

This case describes longitudinal qualitative brain perfusion SPECT findings in a patient with persistent cognitive complaints and a history of mercury exposure. At the initial evaluation, he reported brain fog, intermittent word-finding difficulty, reduced concentration, and decreased work efficiency. Depressive symptoms were minimal on the Patient Health Questionnaire-9, a validated measure of depressive symptom severity [6], and computerized attention testing using the Conners Continuous Performance Test, a standardized measure of sustained attention and response control [7], did not identify an atypical pattern suggestive of an attention-deficit disorder. The initial resting and concentration SPECT studies were clinically interpreted as showing multiple regional differences in relative tracer distribution. On repeat resting imaging approximately eight months later, several previously described relative decreases, including those involving the inferior orbitofrontal, temporal, and frontoparietal regions, were described as less pronounced. The patient subsequently reported modest subjective improvement, although cognitive symptoms remained variable. These parallel clinical and imaging changes are descriptive observations and do not establish that the SPECT findings reflected clinical recovery or that either the symptoms or imaging findings were attributable to mercury exposure.

Mercury can affect the nervous system, although the nature and severity of toxicity depend substantially on the chemical form of mercury, route and magnitude of exposure, and duration of exposure [1,2]. Elemental mercury vapor can cross the blood-brain barrier before oxidation to inorganic mercury, and proposed mechanisms of neurotoxicity include disruption of thiol- and selenol-dependent proteins, oxidative stress, mitochondrial dysfunction, and altered cellular signaling [1]. Clinically significant elemental mercury exposure has been associated with tremor, impaired coordination, mood and behavioral changes, and neuropsychological abnormalities involving domains such as attention, memory, and psychomotor performance [2,8]. These observations provide biological plausibility for neurological and cognitive symptoms in sufficiently exposed individuals; however, such manifestations are nonspecific and cannot, by themselves, establish mercury as the cause of cognitive complaints in an individual patient.

Dental amalgam, a restorative material containing elemental mercury combined with other metals, can release low levels of mercury vapor and therefore represents a source of elemental mercury exposure [9]. However, evidence from human studies does not support inferring clinically significant neurological injury from the presence of dental amalgam alone. In an observational study of 1,663 adult veterans, amalgam exposure was not associated with clinically evident neurological abnormalities or peripheral neuropathy [10]. Two randomized pediatric trials similarly found no significant adverse neuropsychological, neurobehavioral, or neurological differences attributable to amalgam restorations over several years of follow-up [11,12]. A prospective Seychelles cohort also found no association between maternal dental amalgam exposure during pregnancy and neurodevelopmental outcomes at five years of age [13]. These populations and exposure circumstances are not directly equivalent to the present patient, but the findings substantially limit any inference that his remote dental amalgam exposure was responsible for his cognitive symptoms. His amalgam history is therefore best regarded as evidence of prior exposure to mercury-containing dental material rather than evidence of mercury toxicity or mercury-related neurological injury.

Post-chelation urinary mercury testing also requires cautious interpretation. DMPS is a dithiol chelating agent that increases urinary mercury excretion and has been used therapeutically in appropriately selected cases of mercury poisoning [14]. However, provoked urinary mercury concentrations vary according to the chelator and collection protocol and lack validated reference ranges for diagnosing mercury toxicity or estimating total-body burden [15,16]. Accordingly, the post-DMPS result in this case was interpreted as increased urinary mercury excretion following chelation rather than as a quantitative measure of total-body or cerebral mercury burden or, by itself, evidence of mercury toxicity.

Published functional neuroimaging data in mercury exposure remain limited and heterogeneous. O'Carroll et al. described abnormal posterior cingulate SPECT activity in a patient with neuropsychiatric sequelae following inorganic mercury exposure despite an unremarkable structural MRI [4], whereas Rhee et al.

reported cerebellar perfusion defects in a patient with mercury vapor intoxication and cerebellar ataxia [5]. Other nuclear imaging studies have evaluated different biological targets. Lin et al., for example, reported differences in striatal dopamine transporter uptake using technetium-99m TRODAT SPECT in occupationally exposed workers [17]. Dopamine transporter imaging is methodologically and biologically distinct from brain perfusion SPECT and should not be interpreted as evidence of a comparable perfusion pattern. Taken together, the available literature does not establish a reproducible mercury-specific regional brain perfusion signature. The regional findings in the present case should therefore be regarded as descriptive and nonspecific rather than as an imaging marker of mercury neurotoxicity.

The longitudinal imaging findings also require cautious interpretation. On repeat resting SPECT, several previously described relative decreases were qualitatively considered less pronounced, while other regional differences persisted or changed in relative prominence. The comparison was based on routine clinical interpretation rather than blinded serial re-analysis or validated quantitative between-session analysis. Although the images were generated using a standardized linear display scale, the numerical display-scale settings, validated regional thresholds, and normative comparator data were not available for retrospective review. The follow-up examination included only a resting acquisition, preventing direct longitudinal comparison with the initial concentration condition. In addition, formal neuropsychological re-testing was not performed, so the relationship between interval imaging differences and the patient's subjective clinical course remains descriptive only. Accordingly, the interval findings should not be interpreted as evidence of normalization, recovery of brain function, reversal of a toxic process, or treatment response [3].

Brain perfusion SPECT also involves exposure to ionizing radiation, which is relevant when considering its role in patients with nonspecific cognitive complaints. Nuclear medicine guidelines describe standard administered activities and radiation dosimetry for technetium-99m HMPAO brain perfusion SPECT, and the use of such imaging should be based on a clinical judgment that the anticipated information justifies the associated radiation exposure [18]. In the present retrospective case, the exact administered radiotracer activity and the original patient-specific risk-benefit assessment were unavailable for independent review. Moreover, the observed SPECT findings were nonspecific and did not establish an etiologic diagnosis. This case therefore should not be interpreted as supporting routine brain perfusion SPECT for suspected mercury exposure or nonspecific cognitive symptoms; rather, it describes findings from imaging that had already been obtained as part of the patient's clinical evaluation.

The clinical course likewise does not support attribution of the interval imaging differences to a specific intervention. Before the repeat SPECT study, the patient had continued several supplements and lifestyle-oriented measures, whereas previously proposed chelation therapy and plasmapheresis had not been initiated. At subsequent follow-up, he reported modest subjective improvement but continued to experience variable brain fog and concentration difficulty, particularly during periods of travel, occupational stress, fatigue, and sleep disruption. He also reported use of an infrared photobiomodulation device and additional supplements. Because several potential influences changed over time and the reported improvement was limited and subjective, the interval SPECT findings cannot be attributed to mercury removal, supplementation, photobiomodulation, or any other individual intervention.

Several limitations should be considered. The patient's cognitive complaints were nonspecific and were not characterized with comprehensive formal neuropsychological testing. Detailed neurological examination findings and a structural brain MRI report were not available for retrospective review. The magnitude and duration of historical mercury exposure could not be quantified retrospectively, and his dental amalgam restorations had been removed approximately four years before presentation. The available mercury measurements were obtained under fundamentally different collection conditions, including a post-DMPS specimen that cannot be interpreted as a conventional exposure or body-burden measurement. The SPECT findings were based on qualitative clinical interpretation rather than validated quantitative regional or between-session analysis, the exact administered radiotracer activity was unavailable for retrospective confirmation, and the follow-up study did not include a concentration acquisition. Multiple concurrent lifestyle, supplement, travel, stress, fatigue, and sleep-related factors further limit any attempt to associate either the clinical course or imaging findings with a single cause.

Despite these limitations, the case provides a longitudinal description of qualitative relative brain perfusion findings in a patient with persistent cognitive symptoms and a history of mercury exposure. Its significance lies in the longitudinal clinical and imaging observations rather than in establishing a distinct mercury-related syndrome. The available evidence does not establish that prior dental amalgam exposure caused the patient's cognitive symptoms, that the SPECT findings represent mercury neurotoxicity, or that the interval imaging differences represent treatment response or removal of mercury from the nervous system. In this setting, brain perfusion SPECT is best regarded as an adjunctive descriptive modality, while exposure history, appropriately interpreted biomarker testing, and conventional neurological and cognitive assessment remain central to clinical interpretation.

Conclusions

This case describes longitudinal qualitative brain perfusion SPECT findings in a patient with persistent cognitive symptoms and a history of mercury-containing dental amalgam exposure. Interval differences in

relative tracer distribution occurred alongside modest subjective improvement, but the available data do not establish that mercury exposure caused the patient's symptoms or imaging findings, nor that the interval changes reflected treatment response or removal of mercury from the nervous system.

The added value of this case lies in its longitudinal description of qualitative perfusion findings together with the interpretive challenges posed by remote exposure history, post-chelation urinary mercury testing, and nonspecific functional imaging. Clinically, remote dental amalgam exposure should not be equated with established mercury toxicity, post-chelator urinary mercury results should not be treated as conventional measures of body burden, and qualitative brain perfusion SPECT should remain an adjunctive descriptive modality rather than a substitute for standard neurological and cognitive assessment.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Binh Pham

Acquisition, analysis, or interpretation of data: Binh Pham

Drafting of the manuscript: Binh Pham

Critical review of the manuscript for important intellectual content: Binh Pham

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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