

# Case Report: A World Trade Center (WTC) responder presenting with moderate stage dementia by age 57, suggesting an extended severity of WTC-associated illness'

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## Case Report

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## Abstract

Recent evidence indicates that World Trade Center Responders (WTCRs) are apparently at increased risk for a clinical syndrome that includes PTSD (posttraumatic stress disorder) and MCI (mild cognitive impairment). The association of these behavioral and cognitive symptoms was first described by Bromet, Luft, Clouston, and colleagues. No autopsy characterization of the syndrome has yet emerged, though biofluid and neuroimaging biomarker data support features of (1) progressive behavioral and cognitive dysfunction, (2) proteinopathy involving the appearance of neurodegeneration-related molecules in the peripheral circulation, and (3) a substantial regional loss of brain volume. Inciting factors such as inhalation of neurotoxins and/or psychological stressors (or a combination of both) have been proposed as contributory to the pathogenesis, but no definitive etiologic agent has been identified. In general, the subpopulation of WTCRs who developed PTSD and MCI were those with documentable extended exposure to the central feature of “Ground Zero” known as “the pile”, and those who developed MCI were primarily a subgroup of those who had developed PTSD. Multiomic studies are underway to determine whether this subgroup might be enriched for genetic, genomic, and/or proteomic features that might have predisposed them to pathological responses to stress, environmental toxins, or both. In 2017, we had occasion to evaluate “E.T.”; at that time, a 57-year-old bilingual (English and Spanish speaking) right-handed WTCR was referred to an urban medical center dementia specialty clinic for assessment of his cognitive and behavioral functioning. While early-onset dementia can occur sporadically, the proximity of E.T. to “the pile” at “Ground Zero”, and the course of E.T.’s illness raise the possibility that WTC-related cognitive-behavioral syndromes may progress well beyond the stage of MCI to that of moderate dementia (and beyond) and that this progression may occur in the absence of full-blown PTSD.

## Case Report

Recent evidence indicates that World Trade Center Responders (WTCRs) are apparently at increased risk for a clinical syndrome that includes PTSD (post-traumatic stress disorder) and MCI (mild cognitive impairment)<sup>1-10</sup>. The association of these behavioral and cognitive symptoms was first described by Bromet, Luft, Clouston, and colleagues<sup>1-3</sup>. No autopsy characterization of the syndrome has yet emerged, though biofluid and neuroimaging biomarker data support features of: (1) progressive behavioral and cognitive dysfunction, (2) proteinopathy involving the appearance of neurodegeneration-related molecules in the peripheral circulation, and (3) a substantial region loss of brain volume<sup>4-8</sup>. Inciting factors such as inhalation of neurotoxins and/or psychological stressors (or a combination of both) have been proposed as contributory to the pathogenesis, but no definitive etiologic agent has been identified<sup>8,9</sup>. In general, the subpopulation of WTCRs who developed PTSD and MCI were those with documentable extended exposure to the central feature of “Ground Zero” known as “the pile”<sup>1-3</sup>, and those who developed MCI were primarily a subgroup of those who had developed PTSD. Multi-omic studies are underway to determine whether this subgroup might be enriched for genetic, genomic, and/or proteomic features that might have predisposed them to pathological responses to stress, environmental toxins, or both<sup>8-10</sup>.

In 2017, we had occasion to evaluate “E.T.”, at that time, a 57-year-old bilingual (English and Spanish speaking), right-handed WTCR referred to an urban medical center dementia specialty clinic for assessment of his cognitive and behavioral functioning. History and background information were obtained through a Clinical Interview with the patient and his wife.

According to E.T.’s wife, E.T.’s neurobehavioral syndrome began with changes in memory in 2013, leading to the diagnosis of early onset dementia in 2014. E.T.’s wife described his frequent repetition of statements or questions within minutes apparently unaware that he had made the same comments or asked the same questions just minutes earlier. She also described progressive word-finding difficulty and spatial disorientation during navigation (e.g., difficulty finding his way home while driving). As a result, E.T. was not permitted to operate a motor vehicle.

E.T.’s wife reported that he had begun to suffer mild depression and anxiety in 2011 but that neither symptom had been serious enough to require psychotropic medication. There was no diagnosis of PTSD, and there were no episodes of flashback re-experiences. There was also no history of stroke, TBI, seizures, or CNS infection. Other medical history included chronic cough, gout, hypothyroidism, benign prostatic hyperplasia, and hypertension. His medications included memantine, aspirin, amlodipine-olmesartan, levothyroxine, colchicine, fish oil, and multivitamins. He and his wife described E.T.’s alcohol intake as “rare” for his entire life, including at the time of the evaluation. There was no history of use or abuse of tobacco or illicit or prescription medications.

E.T.’s family history was significant for coronary disease in both father and mother, diabetes (mother), and hypertension (mother). Both mother (age 72 yrs) and father (age 82 yrs) were living when E. T. was assessed neurologically. There is no known history of dementia in any members of E.T.’s family.

E. T. was born in Ecuador, and Spanish was his first language. He moved to the United States when he was five years old and learned English in US schools. There was no history of learning disability in childhood. He graduated from High School and completed three years of college. He joined the United States Marine Corps and was stationed in Parris Island, South Carolina. No recognized military-associated toxin exposure or battlefield engagement was included in E.T.’s Marine Corps service. He subsequently worked as a correction officer for approximately ten years, and as a police officer at the New York Police Department (NYPD) for another ten years.

E.T. was among the first responders at the World Trade Center Attacks on 09/11/2001, and he subsequently spent about three months as a supervisor of the digging operations at “Ground Zero” as part of his duty at the NYPD. He was routinely present near “the pile” where the WTC fell and where he was potentially exposed to aerosolized silicates and organic compounds. He retired from the NYPD in 2005 and worked as a ticket enforcement officer for the New York Metro Transit Authority until 2013, when he retired due to his cognitive impairment. E.T. reported using both English and Spanish daily and preferred to be tested in English. He had three children and three grandchildren from his first marriage. Details of the first marriage were not recorded or available. E.T.’s second marriage took place in 2016, soon before he was seen in our clinic. E.T. and his wife and son were living on Staten Island.

The following tests were used to assess areas of intellect, premorbid abilities, language, memory, learning, visuospatial abilities, executive functioning, motor ability and processing speed: Record Review; Clinical Interview; Beck Anxiety Inventory (BAI); Beck Depression Inventory (BDI); Dementia Rating Scales second edition (DRS-2); Texas Functional living Scale (TFLS); and Vineland Adaptive Behavior Scales.

E.T. arrived at the neuropsychological testing appointment well-groomed, appropriately dressed, and was oriented only to person. His attention span was normal. Stimulus bound behaviors and mild impulsivity were observed during testing. Language comprehension appeared to be within normal limits, though repetition of questions and test instructions was often required. Pitch, prosody, and volume of speech were normal. Rate of speech was slow due to hesitation and anomia. His affect was sad and anxious, and he required multiple encouragements to complete the testing session. Overall, E.T. apparently put forth full effort on all tests administered.

E.T.'s premorbid intellectual abilities were estimated to fall within normal limits. In contrast, his current performance fell well below the cut-point required to support for a diagnosis of dementia. His MMSE was < 20. His Dementia Rating Scale-2 (DRS-2) Total was below the 1<sup>st</sup> percentile.

In terms of emotional status, E.T.'s responses on self-report mood inventories were not indicative of clinical levels of depression (BDI = 5) or anxiety (BAI= 2). Therefore, neither by history from his wife nor from observation and examination, PTSD was not part of the clinical picture.

In terms of activities of daily living, E.T. was unable to demonstrate his understanding of concepts of time and money calculations on a test of functional living, and he could not follow-up on a simple task following a 5-minute delay. Consistent with these pervasive adaptive function deficits, as indicated by responses on a questionnaire completed by his wife, E.T. was incapable of self-care, including an inability to manage finances, navigation, and day/night orientation.

[<sup>18</sup>F]fluorodeoxyglucose positron emission tomography (FDG-PET; Figure) revealed bilateral temporoparietal hypometabolism consistent with the metabolic signature of Alzheimer's disease.

Progressive neurological and psychiatric decline continued until E.T. died at age 59 yrs from symptoms that were attributed to acute pulmonary edema but occurred in May, 2020, in the context of the COVID-19 pandemic.

Taken together, E.T.'s performance on this evaluation was marked by widespread cognitive difficulties, especially in the domains of attention, memory, executive functioning, and tasks of functional living. The range and scope of E.T.'s cognitive and adaptive functioning changes were used to justify a DSM-5 diagnosis of "Major Neurocognitive Disorder, without Behavioral Disturbance".

Estimated scaling of E.T.'s cognitive impairment (MMSE<20 and DRS-2 below the 1<sup>st</sup> %ile) indicated that his level of impairment progressed in severity substantially beyond that encompassed by the diagnosis of MCI and was well within the range associated with moderate dementia. While early onset dementia can occur sporadically, the proximity of E.T. to "the pile" at "Ground Zero", and the course of E.T.'s illness raises the possibility that WTC-related cognitive-behavioral syndromes may progress well beyond the

stage of MCI to that of moderate dementia (and beyond) and that this progression may occur in the absence of full-blown PTSD. Despite the absence of autopsy neuropathology from any WTC-related cognitive-behavioral syndrome patient, progress in our understanding of the biomarker and multi-omic characterization of neurodegenerative diseases in general and of WTC-related cognitive-behavioral syndromes in particular should inform the determination of which features of neurodegeneration, proteinopathy, and/or neuroinflammation contribute to WTC-related cognitive-behavioral syndromes. This knowledge, in turn, could facilitate the design of clinical trials aimed at preserving cognitive and behavioral function in WTC-related cognitive-behavioral syndromes.

## Abbreviations

WTCR	World Trade Center Responder
PTSD	Post-traumatic stress disorder
MCI	Mild cognitive impairment

## Declarations

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### Ethics approval and consent to participate

N/A clinical case report, postmortem

### Consent for publication

Consent to publish patient details has been provided by his next of kin

### Availability of data and material

N/A

### Competing interests

None

### Funding

Described above

### Authors' contributions

S.G., T.A., and H.A.B. wrote the first draft of the manuscript. J.C., R.G.L., E.J.B., S.A.P.C., and M.S. edited the manuscript. B. J. L. directs the WTC Program at the Renaissance School of Medicine at Stony Brook University.

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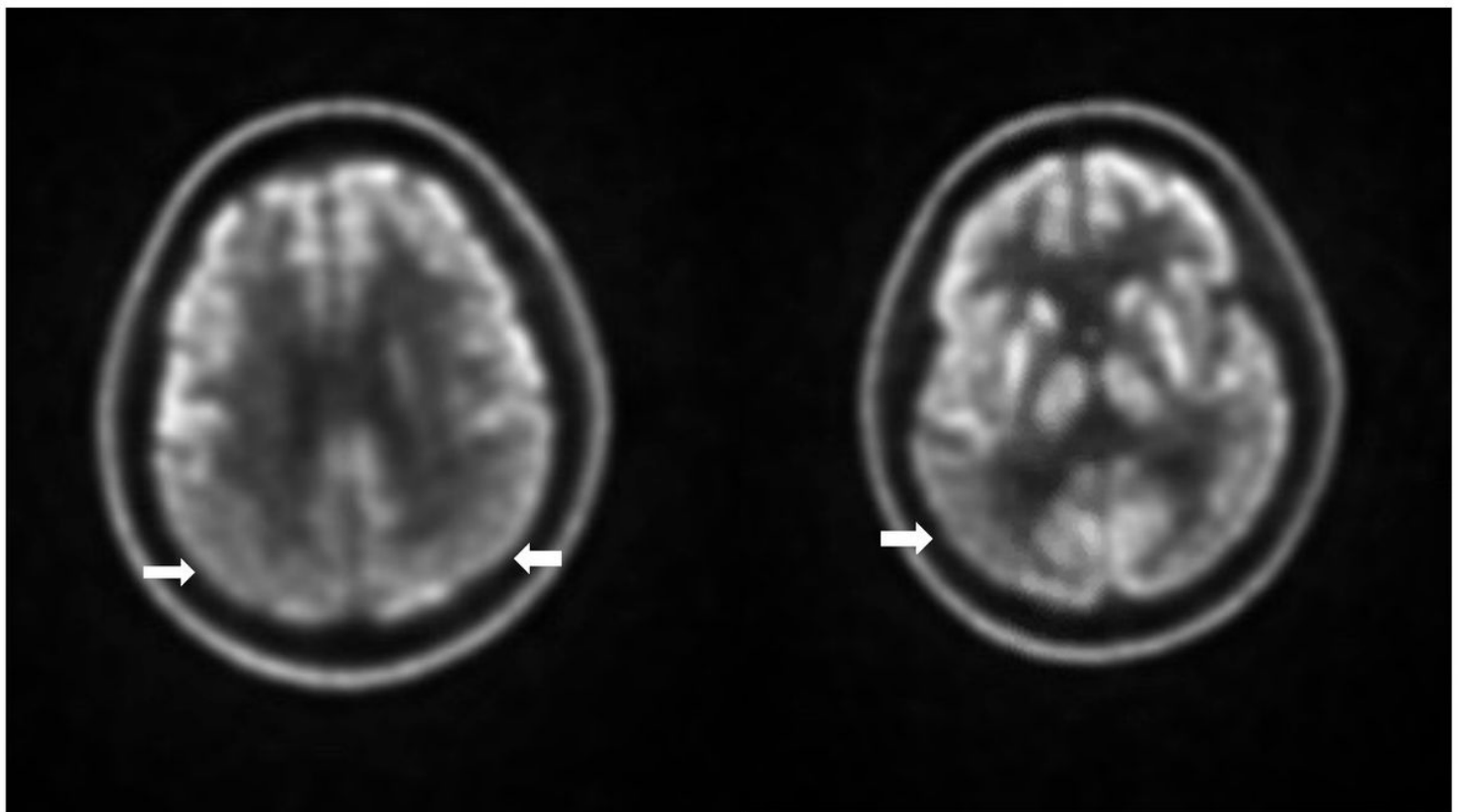
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## Figures



**Figure 1**

Selected brain metabolic [<sup>18</sup>F]fluorodeoxyglucose positron emission tomography (PET) images from patient E.T., a WTC responder who developed moderate stage dementia by age 57 in the absence of a diagnosis of PTSD. Both images show the metabolic signature of asymmetrical bilateral parietal hypometabolism (arrows) interpreted as consistent with a diagnosis of early onset Alzheimer’s disease (AD).