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# JP8 exposure and neurocognitive performance among US Air Force personnel

Kristin J. Heaton[a,b], Alexis L. Maule[a,b,c], Kristen W. Smith[b,d], Ema G. Rodrigues[b,d], Michael D. McClean[b], Susan P. Proctor[a,b,e,*]

[a] Military Performance Division, US Army Research Institute of Environmental Medicine, 10 General Greene Avenue, Natick, MA 01760, USA
[b] Department of Environmental Health, Boston University School of Public Health, 715 Albany Street, Boston, MA 02118, USA
[c] Henry M. Jackson Foundation, 6720A Rockledge Dr. #100, Bethesda, MD 20817, USA
[d] Department of Environmental Health, Harvard T.H. Chan School of Public Health, 677 Huntington Avenue, Boston, MA 02115, USA
[e] Research Service, VA Boston Healthcare System, 150 South Huntington Ave., Boston, MA 02130, USA

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ABSTRACT

Petroleum-based fuels such as jet propellant (JP) 4, JP5, JP8, and jet A1 (JetA) are among the most common occupational chemical exposures encountered by military and civilian workforces. Although acute toxicity following high-level exposures to JP8 and similar chemical mixtures has been reported, the relationship between persistent low-level occupational exposures to jet fuels and both acute and longer-term central nervous system (CNS) function has been comparatively less well characterized. This paper describes results of neurocognitive assessments acquired repeatedly across a work week study design (Friday to Friday) as part of the Occupational JP8 Exposure Neuroepidemiology Study (OJENES) involving U.S. Air Force (AF) personnel with varying levels of exposure to jet fuel (JP8). JP8 exposure levels were quantified using both personal air monitoring and urinary biomarkers of exposure. Neurocognitive performance was evaluated using an objective, standardized battery of tests. No significant associations with neurocognitive performances were observed between individuals having regular contact and those with minimal/no direct contact with JP8 (measured by average work week levels of personal breathing zone exposure). Also, no significant findings were noted between repeated measures of absorbed dose (multi-day pre-shift urinary 1- and 2-naphthol) and reduced proficiency on neurocognitive tasks across the work week. Results suggest that occupational exposure to lower (than regulated standards) levels of JP8 do not appear to be associated with acute, measurable differences or changes in neurocognitive performance.

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## 1. Introduction

Petroleum-based fuels such as jet propellant (JP) 4, JP5, JP8, and jet A1 (JetA) are among the most common occupational chemical exposures encountered by military and civilian workforces. Routine occupational exposures involving military and commercial personnel may involve handling of jet fuel on a daily basis over the course of many years. Acute toxicity following high-levels of exposure to raw fuel products, fuel vapor/aerosol, or products of fuel combustion have been described previously for both animals and humans (Carlton and Smith, 2000; Ritchie et al., 2003; Smith et al., 1997). However, the effects of persistent lower level occupational exposure over time (across a work week or across many years) to jet fuels on central nervous system (CNS) function have been, by comparison, less well characterized.

Current exposure guidelines for jet fuel, established by the American Conference of Governmental Industrial Hygienists (American Conference of Governmental Industrial Hygienists (ACGIH), 2013), have been set at an 8-h time weighted average (TWA) of 200 mg/m$^3$ for total hydrocarbons. These limits were established, in part based on known effects on CNS and peripheral nervous system (PNS) observed in both animals and humans exposed to levels of fuels exceeding this threshold (Anger, 1984). JP8 contains more than 200 aliphatic and aromatic solvent

* Corresponding author at: Military Performance Division, US Army Research Institute of Environmental Medicine, 10 General Greene Ave., Bldg. 42 Natick, MA 01760, USA.
*E-mail addresses:* kristin.j.heaton.civ@mail.mil (K.J. Heaton), alexis.l.maule.ctr@mail.mil (A.L. Maule), kristen.weida.smith@gmail.com (K.W. Smith), emarod77@yahoo.com (E.G. Rodrigues), mmcclean@bu.edu (M.D. McClean), susan.p.proctor.civ@mail.mil (S.P. Proctor).

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compounds and a variety of nonhydrocarbon performance additives (Agency for Toxic Substances and Disease Registry (ATSDR), 2017; National Research Council (NRC), 2003). The organic solvents that are major components of JP8 and other fuels, such as benzene, ethylbenzene, toluene, xylene, and naphthalene, have known adverse effects on the human CNS and PNS resulting in neurobehavioral deficits, including degraded motor, learning, memory, attention, and visual-spatial performance, and reductions in processing speed (Bælum et al., 1985; Echeverria et al., 1991; Foo et al., 1990; Lotti and Bleecker, 2015; Meyer-Baron et al., 2008; Olson et al., 1985; Sainio, 2014; van Valen et al., 2012). The specific effects on CNS function depend largely on the chemical composition of the solvent mixture, the level of exposure and its duration (Sainio, 2014). In some cases, a brain syndrome known as chronic solvent encephalopathy (CSE) has been observed, characterized by impairments in attention, memory, motor performance and information processing speed and is often accompanied by neuropathological changes as observed on brain imaging (van Valen et al., 2012). (Pleil et al., 2000; Puhala et al., 1997). (Meyer-Baron et al., 2008). Although considered a safer fuel alternative than earlier jet fuel formulations (such as JP4 and JP5), JP8′s reduced volatility relative to other jet fuels (National Research Council (NRC), 2003) increases its persistence on skin and clothing, extending the possible duration of exposure and, relatedly, possible exposure dose (Pleil et al., 2000; Puhala et al., 1997).

Acute exposures to JP8 at levels near or exceeding 350 mg/m$^3$ and exceeding current exposure guidelines (i.e., 200 mg/m$^3$) have been shown in both animal and in vitro toxicological studies to negatively impact immune, respiratory, and nervous system functions (National Research Council (NRC), 2003). Dizziness, headache, nausea, mental confusion, slurred speech, fatigue and gait instability have also been reported following acute JP8 exposure (Carlton and Smith, 2000; Smith et al., 1997). Moreover, persistent exposure (estimated to be 300 mg/m$^3$ over 17 years on average) in humans to earlier formulations of jet fuel (MC-77, Swedish military fuel equivalent to JP-4) has been associated with dizziness, headache, nausea, neurasthenia, polyneuropathy (e.g., distal paresthesia and numbness, or paresis), and neurocognitive deficits primarily involving psychomotor speed and visual perceptual speed (Knave et al., 1979, 1978, 1976). More recently, subtle (subclinical) shifts in neurocognitive performance were observed between U.S. Air Force (AF) personnel with higher and lower levels of expected exposure to JP8 based on job category at the start of and across a 4–6 h work shift (Anger and Storzbach, 2001). In particular, workers in the higher exposure group compared to lower exposure group performed less well on neurocognitive tasks involving working memory (number sequence recall), psychomotor speed (coding), and motor skills. Across the work shift (from pre- post), those exposed to higher levels of naphthalene demonstrated significant changes in visuospatial memory and motor speed (tapping) performance relative to a comparison group of lower naphthalene exposed individuals. Subtle differences in reaction time and response accuracy have also been noted in Air National Guard personnel exposed to higher levels of JP8 (but below regulated exposure guidelines) as measured by exhaled breath sampling and based on job category (e.g., fuel cell workers) relative to those with expected lower levels of exposure to fuels (e.g., supply workers) (Tu et al., 2004).

In this paper we examine the results of neurocognitive performance assessments acquired repeatedly across a standard work week with AF personnel who, as a function of their specific job characteristics, had higher or lower levels of exposure to jet fuel. This study, known as the Occupational JP8 Exposure Neuroepidemiology Study (OJENES), (Proctor et al., 2011) implemented objective and individual-level measures of JP8 exposure within the context of a prospective research design. Sampling was conducted repeatedly across an entire work week, permitting analysis of whether average exposure dose as well as day-to-day exposure fluctuations influence key neurocognitive performance outcomes. Several papers have been published from the OJENES that provide detailed characterization of the individual-level exposure assessment methods and findings (Maule et al., 2016; Merchant-Borna et al., 2012; Rodrigues et al., 2014; Smith et al., 2010, 2012). In this study, we have two primary aims with respect to the effect of JP8 exposure on neurocognitive performance. First, we examined the relationship between objectively measured personal JP8 exposure and neurocognitive performance, hypothesizing that higher compared to lower or no personal exposure to occupational JP8 was associated with negative neurocognitive performances. Second, we predicted that higher, compared to lower, levels of JP8 repeatedly measured over a work week as determined by urinary biomarker levels of 1- and 2-naphthol would be significantly related to poorer neurocognitive functioning. We also examined the effect of length of AF service and JP8 exposure on neurocognitive performance outcomes to assess whether or not more years of service at higher exposure levels affected performance.

## 2. Materials and methods

The study protocol was approved by institutional review boards at the US Army Research Institute of Environmental Medicine, USAF Research Laboratory at Wright Patterson Air Force Base and Boston University, and was in compliance with human subjects review procedure at the Centers for Disease Control and Prevention. All participants provided written informed consent prior to participation.

### 2.1. Study design and procedures

Proctor and colleagues (Proctor et al., 2011) provide a detailed description of the design and methods of the consecutive 6-day study. In summary, participants were recruited from three AF bases and were eligible to participate if they did not have a self-reported history of loss of consciousness for more than 20 min or known neurological or psychological disorder(s). The recruitment process for this study was designed so that the study sample population included personnel with a range of exposures to JP8 based on their primary job activities. Individuals whose job activities involved routine exposure to JP8 (e.g., fuel cell repair and maintenance) were categorized as high exposure and those whose jobs did not involve routine contact with JP8 (e.g., medical technicians, administration) were categorized as low exposure. In this study, 38 of the 74 participants were considered to be in the high exposure group due to their job description and 36 were classified as being in the low exposure group as they had little-to-no regular direct exposure to JP8 as a part of their job tasks. Data collection at each of the three AF base study sites (n = 21 at A, n = 20 at B, n = 33 at C) began at the end of each participant's work shift on a Friday afternoon (Day 1) and continued Monday morning through Friday morning of the following work week (Days 2–6).

All participants were given a brief neurological screening examination by a trained examiner in order to assess the presence of any potential neurologic impairment. As part of the study, questionnaires were administered to gather demographic information (e.g., age, sex, and education level), lifestyle behaviors (e.g., smoking and alcohol use), work history (e.g., current job, length of AF service), daily work activities (e.g., job tasks, workday schedule,