Elevated neutrophil to lymphocyte ratio in older adults with cocaine use disorder as a marker of chronic inflammation

Supplemental material: Full medical exclusionary criteria materials

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Inflammatory Marker Checklist

Requirements

_____ **No current or past TB**

_____ **HIV negative per self-report**

_____ **No hepatitis C diagnosis per self-report**

_____ **No other significant medical conditions (see "Exclusionary Criteria for Borderline Conditions")**

Common concerns:
- Any type of arthritis
- Asthma
- GERD
- COPD

_____ **Not pregnant, breastfeeding, or currently taking oral contraceptives**

_____ **No prescribed anti-inflammatories or regular over-the-counter anti-inflammatory use**

_____ **No schizophrenia or other psychotic disorder diagnosis**

Other disorders *included*:
-generalized anxiety disorder
-major depressive disorder

_____ **Cocaine dependence diagnosis**

Exclusionary Criteria for Borderline Conditions

For conditions which have spectrums of inflammation are Diabetes Mellitus (DM), Hypertension, and Hyperlipidemia, clinical judgement was used per the following criteria.

Cases were excluded if:

- Client reports DM **and** they are taking DM medications
- Glucose from LabCorp is $\geq$ to 126, regardless of treatment
- Client reports Hypertension and they are taking an anti-hypertensive
    - If no medication for Hypertension then the Metabolic Syndrome Criteria was assessed (see below)
- Client reports any type of Hyperlipidemia and they are taking medication

- If no medication for Hyperlipidemia then the Metabolic Syndrome Criteria was assessed (see below)

Metabolic Syndrome Criteria from ATPIII

Below is the official criteria for Metabolic Syndrome. As our dataset did not have all the required numbers, such as waist circumference, we used working definitions, noted underneath the official criteria. Meeting 3 out of the 5 criteria defined someone as having metabolic syndrome.

- ●Abdominal obesity, defined as a waist circumference in men ≥102 cm (40 in) and in women ≥88 cm (35 in)
  - **We used BMI >= 30.**
- ●Serum triglycerides ≥150 mg/dL (1.7 mmol/L) or drug treatment for elevated triglycerides
  - **We only used the LabCorp triglyceride values as being part of the criteria as drug treatment is an automatic exclusion.**
- ●Serum high-density lipoprotein (HDL) cholesterol <40 mg/dL (1 mmol/L) in men and <50 mg/dL (1.3 mmol/L) in women or drug treatment for low HDL cholesterol
  - **We only used the LabCorp Total Cholesterol values > 200 as we did not have HDL values. Drug treatment for hyperlipidemia was an automatic exclusion.**
- ●Blood pressure ≥130/85 mmHg or drug treatment for elevated blood pressure
  - **We only used the blood pressure values as drug treatment was an automatic exclusion. Either the systolic or diastolic can be elevated for meeting this criteria.**
- ●Fasting plasma glucose (FPG) ≥100 mg/dL (5.6 mmol/L) or drug treatment for elevated blood glucose
  - **We only used the LabCorp Glucose values as drug treatment is an automatic exclusion. Here a value between 100 and 125 inclusive met the criteria. A value greater than or equal to 126 was automatically exclusionary**.

Exclusion Criteria for Medications

The following table lists medications that were exclusionary for the current study. An M.D. and medical student reviewed potential medications and determined which should be excluded. Note that MISC = miscellaneous.

Supplementary Table 1. Exclusionary Medications					
ANTI-INFECTIVES	MISC ANTIFUNGALS	RIFAMYCIN DERIVATIVES	HYDRAZIDE DERIVATIVES	ADAMANTANE ANTIVIRALS	ANT-IVIRAL CHEMOKINE RECEPTOR ANTAGONIST
ANTI-FUNGALS	ANTI-MALARIAL QUINOLINES	MISC ANTI-TUBERCULOSIS AGENTS	PROTEASE INHIBITORS	PURINE NUCLEOSIDES	INTEGRASE STRAND TRANSFER INHIBITOR
ANTI-MALARIAL AGENTS	AZOLE ANTI-FUNGALS	ANTI-TUBERCULOSIS COMBINATIONS	NRTIS	NEURAMINIDASE INHIBITORS	FIRST GENERATION CEPHALOSPORINS
ANTI-TUBERCULOSIS AGENTS	MISC ANTI-MALARIALS	MACROLIDES	MISC ANTI-VIRALS	ANTI-VIRAL COMBINATIONS	SECOND GENERATION CEPHALOSPORINS
ANTI-VIRAL AGENTS	ANTI-MALARIAL COMBINATIONS	KETOLIDES	NNRTIS	ANTI-VIRAL INTERFERONS	THIRD GENERATION CEPHALOSPORINS
LEPROSTATICS	PENICILLINASE RESISTANT PENICILLINS	QUINOLONES	LINCOMYCIN DERIVATIVES	LINCOMYCIN DERIVATIVES	MISC ANTI-NEOPLASTICS
MACROLIDE DERIVATIVES	ANTI-PSEUDOMONAL PENICILLINS	SULFONAMIDES	GLYCOPEPTIDE ANTIBIOTICS	OTHER IMMUNO-STIMULANTS	MITOTIC INHIBITORS
MACROLIDE DERIVATIVES	AMINO-PENICILLINS	TETRACYCLINES	ALKYLATING AGENTS	ANTINEOPLASTIC HORMONES	ANTINEOPLASTIC INTERFERONS
MISC ANTIBIOTICS	BETA-LACTAMASE INHIBITORS	URINARY ANTI-INFECTIVES	ANTI-METABOLITES	RESPIRATORY INHALANT PRODUCTS	ANTINEOPLASTIC DETOXIFYING AGENTS
PENICILLINS	NATURAL PENICILLINS	AMINO-GLYCOSIDES	ANTINEOPLASTIC HORMONES	PSYCHO-THERAPEUTIC AGENTS	MULTIKINASE INHIBITORS
ANTI-NEOPLASTICS	BCR-ABL TYROSINE KINASE INHIBITORS	CORTICOTROPIN	RESPIRATORY AGENTS	IMMUNOLOGIC AGENTS	INHALED CORTICO-STEROIDS
CENTRAL NERVOUS SYSTEM AGENTS	VEGF/VEGFR INHIBITORS	GLUCO-CORTICOIDS	IMMUNO-SUPPRESSIVE AGENTS	ANTIPSYCHOTICS	TNF ALFA INHIBITORS
ANALGESICS	EGFR INHIBITORS	MINERALO-CORTICOIDS	IMMUNO-STIMULANTS	IMMUNE GLOBULINS	INTERLEUKIN INHIBITORS
NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	HER2 INHIBITORS	ANDROGENS AND ANABOLIC STEROIDS	MISC ANTIPSYCHOTIC AGENTS	MISC BIOLOGICALS	SELECTIVE IMMUNOSUPPRESSANTS
SALICYLATES	PROTEASOME INHIBITORS	IMMUNOLOGIC AGENTS	PSYCHO-THERAPEUTIC COMBINATIONS	IMMUNOSUPPRESSIVE AGENTS	OTHER IMMUNOSUPPRESSANTS
ANALGESIC COMBINATIONS	COX-2 INHIBITORS	CALCINEURIN INHIBITORS	PHENOTHIAZINE ANTIPSYCHOTICS	ATYPICAL ANTIPSYCHOTICS	COLONY STIMULATING

					FACTORS
HORMONES/ HORMONE MODIFIERS	ADRENAL CORTICAL STEROIDS	METABOLIC AGENTS	THIOXANTHENES	SEX HORMONES	INTERFERONS
ANTIGOUT AGENTS					

Variable Harmonization

Age, race, and gender were determined by standard self-report methods. For estimated income data, NHANES respondents were asked to report total family income for themselves and the other members of their family, received last month in dollars. Family monthly income was reported as a range of values in dollars. The response categories were (by upper limit): $0-$399, $400, $800, $1250, $1650, $2100, $2900, $3750, $4600, $5400, $6250, $8400 and above. CUD participant income data was obtained from the Addiction Severity Index, ASI[50)]. Similar to the NHANES, participants reported total family/household income received from all sources. The response categories were (by upper limit): $0-399, $800, $1250, >$1250. The NHANES data were subsequently recoded to match the CUD (ASI) data and create identical income categories for data analysis.

Data collection methods regarding substance use patterns between the NHANES and ASI datasets were sufficiently different that alcohol, nicotine, and marijuana use data required harmonization into binary response categories (current user vs. non-user). For the ASI data, alcohol use (beer, hard liquor, wine) in the past month and year were used to estimate annual usage. If the estimated number of drinking occasions per 12 months was ≥ 12 / < 12, respondents were coded as alcohol users / non-users, respectively. For the NHANES data, alcohol use was reported as frequency per week, month, or year (as appropriate). These data were used to estimate annual usage and occasions per 12 months with ≥ 12 / < 12 used to code users / non-users, respectively, to match the ASI estimates. Reports coded in the NHANES dataset as “Don’t

Know" or "Refused" or "Missing" were coded as missing. ASI data for marijuana use frequency, times used in the past 30 days was used to code the participant as a current-user or non-user. NHANES data from use of marijuana or hashish in the past 30 days was used similarly to code the respondent as a current marijuana user or non-user. For CUD nicotine use, data were obtained from intake medical screening documents and based on number of cigarettes per day in half-pack increments. Those reporting 0 ("I never smoke cigarettes") on the medical screen were coded as non-smokers and those reporting 1-6 ("occasionally smoke cigarettes" to "smoke 3 packs per day") were coded as smokers. NHANES data for nicotine use was determined from reports of "Every Day", "Some Days", or "Not at all" to code respondents as a user or non-user. Reports coded in the NHANES dataset as "Don't Know" or "Refused" or missing were coded as missing. Data were harmonized by categorizing individuals both datasets as 0 (non-smoker) or 1 (smoker).

Race was initially obtained in standard categories, as per NIH NOT-15-089 (https://grants.nih.gov/grants/guide/notice-files/not-od-15-089.html): American Indian or Alaska Native, Asian, Black or African American, Hispanic or Latino, Native Hawaiian or Other Pacific Islander, White. Due to 0 to < 3 observations in several categories in the CUD group, categories were collapsed into Black, White, and Other (n = 7). For the NHANES dataset, the same standard NIH categories were present in the NHANES dataset, but were collapsed into Black, White, and Other in order to harmonize the datasets for analysis.