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Case Reports

Safety, Science, or Both? Deceptive Healthy Volunteers: Psychiatric Conditions Uncovered by Objective Methods of Screening

Adriana Pavletic, M.D., Ph.D., Maryland Pao, M.D.

Introduction

Healthy volunteers (HVs) play an important role in psychiatric research. They provide scientists with valuable information for comparison with patients who have mental disorders, or who serve as participants in studies of healthy brain anatomy and physiology, such as attention, perception, and memory. Previous reports document a high prevalence of psychopathology among HVs (16–44%) and highlight the importance of mental health screening of HVs.[1–4]

Psychiatric research has typically used rating scales and clinical interviews (e.g., structured clinical interview)[5] to rule out psychopathology. These instruments rely on the assumption that the information provided by HVs is accurate. However, it is well known that some volunteers use deception owing to financial incentive or other reasons.[6–12] Compared to medical conditions, psychiatric disorders are easier to conceal as they do not have biomarkers, and they often have no signs. For example, in a phase 1 clinical trial, 34% of exclusions were due to psychiatric disorder, alcohol, or drug problem, and 72% of these exclusions were concealed and discovered owing to the information provided by volunteers' general practitioner.[13] Concealment of psychiatric disorders not only affects the integrity of research but has also had tragic consequences.[14,15]

Compared to patients, HVs are frequently less rigorously screened, which may affect research outcome.[1,16] A multicenter comparison analysis found larger variability in cerebrospinal fluid biogenic amines among controls than among patients, possibly owing to inadequate screening of HVs.[16]

Although psychiatric research involving HVs relies on participants without medical conditions that might affect their safety or the function of the brain, medical screening of HVs is rarely discussed.[17] Shtasel et al.[1] excluded 46% of HVs due to psychiatric or medical conditions but did not describe medical exclusions. Researchers who are developing an MRI atlas of a healthy human brain excluded 48% of participants due to findings on history and physical examination.[18] Most of the excluded volunteers were above age 60 and had hypertension or neurological abnormalities.[18] The same authors reported that only 7.4% out of 474 neuroimaging studies included a physical examination in screening of HVs.[18]

From our cohort of 476 HVs (mean age 27 ± 8 years), we excluded 18% of participants owing to medical or psychiatric problems.[17] Volunteers applied for various studies including functional magnetic resonance imaging, fear conditioning with electric shocks, and psychopharmacology protocols.[17] In addition to unknown or undisclosed medical conditions (e.g., severe hypertension), medical screening detected psychiatric problems that HVs concealed during the mental health evaluation.[17] Here, we describe 9 illustrative cases that were uncovered by a physical examination, laboratory testing, toxicology screening, and chart review (i.e., objective methods). All volunteers had a negative structured clinical

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From the National Institute of Mental Health, Office of the Clinical Director, Bethesda, Maryland 20892, USA. Send correspondence and reprint requests to Adriana Pavletic, M.D., Ph.D.; e-mail: pavletia@mail.nih.gov

interview and a self-reported negative psychiatric history.

Case Presentations

Physical Examination and Chart Review

Case 1—Extremely Severe Anorexia Nervosa

A 34-year-old college-educated, employed woman presented as a HV to determine eligibility for a fear conditioning study. She stated that her motivation to participate in psychiatric research was to give back to the research hospital where her mother had received cancer treatment. She reported 3 kg weight loss due to a recent food poisoning but denied medical illnesses, calorie reduction, binging, purging, excessive exercise, amenorrhea, or history of eating disorders. Physical examination revealed height of 164.5 cm, weight of 38.8 kg, and a body mass index of 14.3 (normal: 18.5–25). Chart review revealed that 10 years earlier, she applied for a study enrolling patients with Cushing syndrome. At that time, she complained of having a fat body and thin extremities although she was approximately 20 kg underweight. She also reported a history of cardiac arrest due to a fall in icy water.

Case 2—Probable Self-Injury by Cutting

A 19-year-old right-handed Asian student was jovial during the interview. Physical examination revealed numerous linear scars on her left forearm. She stated that she accidently cut her arm while babysitting her brother because his crib was sharp. When asked if her brother was also hurt, she said that his side of the crib was padded.

Case 3—Probable Skin Excoriation Disorder Caused by Compulsive Finger Biting

A 25-year-old African American student had loss of pigment, excoriations, and skin thickening on distal aspects of his thumbs that were differently shaped. He had an implant on his front upper tooth that was reportedly extracted due to an abscess. His dentition was otherwise good. When asked about his skin changes, he said that he has been biting on his thumbs since adolescence but denied any distress or impairment in functioning. He added that he used to bite all his fingers but quit "as they became deformed."

Case 4—Cocaine Use Presenting as Severe Hypertension

A 32-year-old man had blood pressure of 202/87 mm Hg. He denied a prior history of hypertension and stated that his systolic blood pressure usually runs at approximately 130 mm Hg. After further questioning, he admitted to recent cocaine use.[17]

Case 5—Probable Past IV Drug Use

A 36-year-old man was found to have small scars and linear and nonlinear hyperpigmented lesions on his forearm. He said that he tends to scar easily and denied ever using drugs. Chart review revealed negative toxicology screens and a chronic hepatitis C infection.

Laboratory Testing and Toxicology Screen

Case 6—Probable Eating Disorder Presenting as Recurrent Hyperkalemia

This case was previously described.[19] A 36-year-old woman had moderately severe hyperkalemia (6.4 nmol/L, repeat 4 hours later 5.8 nmol/L, reference range: 3.3–5.2 nmol/L), and the psychiatrist obtained an internal medicine consult. The internist concluded that her hyperkalemia was likely caused by excessive ingestion of potassium-rich dried fruits. She was informed about the dangers of hyperkalemia and advised to limit her potassium intake. Her potassium level was normal the following day, and she was admitted into a study as a HV. Subsequent evaluation for a different study revealed surprising hyperkalemia. When informed about the result, she stated that she had eaten 1 pound of dried figs the previous night.[19]

Case 7—Cocaine Use and Chronic Hepatitis C

A 42-year-old, college-educated woman reported a distant history of cocaine use that did not meet the criteria for substance abuse. She reportedly stopped using cocaine 7 years earlier when she became pregnant and denied recent drug use. She was unemployed and lived with her healthy 6-year-old son. When asked