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Safety, Science or Both?:

Deceptive Healthy Volunteer: Psychiatric Conditions Uncovered by Objective Methods of Screening

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Abstract

Previous reports document a high prevalence of psychopathology and highlight the importance of mental health screening of healthy volunteers in psychiatric research. Psychiatric research has typically used self-report scales and structured clinical interviews to rule out psychopathology. These subjective methods are often unreliable as some volunteers conceal their psychiatric conditions and substance use. Here we describe illustrative cases of psychiatric conditions in healthy volunteers that were uncovered by objective methods of screening including physical exam, laboratory testing, toxicology screen, and chart review.

Keywords

healthy volunteer; psychiatric research; deception; physical exam; toxicology screen

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 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 structured clinical interviews (e.g., SCID) (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 due to financial incentive or other reasons (6–12). Compared to medical

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Conflict of interest

The authors declare no conflict of interest

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conditions, psychiatric disorders are easier to conceal as they don't have biomarkers and they often have no signs. For example, in one 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 due 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 and colleagues excluded 46% of HVs due to psychiatric or medical conditions but did not describe medical exclusions (1). Researchers who are developing an MRI atlas of a healthy human brain excluded 48% of participants due to findings on history and physical exam (H&P) (18). The majority of excluded volunteers were over 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 exam in screening of HVs (18).

From our cohort of 476 HVs (mean age 27+/- 8 years) we excluded 18% of participants due to medical or psychiatric problems (17). Volunteers applied for various studies including functional magnetic resonance imaging (fMRI), 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 nine illustrative cases that were uncovered by a physical exam, laboratory testing, toxicology screen, and chart review (i.e., objective methods). All volunteers had a negative SCID and a self-reported negative psychiatric history.

Case presentations

Physical exam and chart review

Case 1- Extremely severe anorexia nervosa—A 34-year-old college-educated, employed female 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, bingeing, purging, excessive exercise, amenorrhea, or history of eating disorders. Physical exam revealed height of 164.5 cm, weight of 38.8 kg and a body mass index (BMI) 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 about 20 kilograms 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 pleasant and jovial during the interview. Physical exam revealed numerous linear scars on her left forearm. She stated that she accidentally 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 which were differently shaped. He had an implant on his front upper tooth which 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 pleasant male had blood pressure of 202/87. He denied a prior history of hypertension and stated that his systolic blood pressure usually runs around 130. After further questioning, he admitted recent cocaine use (17).

Case 5 - Probable past IV drug use—A 36-year-old male 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 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 female 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 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 one pound of dried figs the previous night (19).

Case 7- Cocaine use and chronic Hepatitis C—A 42-year-old pleasant college educated female 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 about her sleep, she stated that she sleeps 3–4 hours as she “was checking on her baby”. She was thin (BMI 19) and her physical exam was otherwise unremarkable. Laboratory testing revealed chronic hepatitis C infection and positive toxicology screen for cocaine. When informed about the results, the volunteer stated that she “will start interferon therapy tomorrow.”

Case 8 - Probable heavy marijuana use—A 33-year-old female with a graduate degree reported infrequent marijuana use (last time was three months ago). Her brother had alcohol and drug dependence. She did not have time for toxicology screen as she had to return to work. The test was performed few weeks later and it was positive for tetrahydrocannabinol (THC). The specific gravity of her urine was 1.001 (i.e., abnormally low).

Chart review

Case 9 - Recurrent depression and heavy alcohol use—A chart review of a 41-year-old HV revealed that one year earlier he had participated in a depression treatment study as a patient with recurrent depression and in an alcohol study with a diagnosis “Heavy social drinker, rule out alcohol dependence.” He said that his psychiatric diagnoses were incorrect and that he assumed that his health information was not accessible to other investigators.

Discussion

Our earlier study described findings on medical screening that led to exclusions of healthy and patient volunteers from psychiatric research (17). This case series illustrates examples of psychiatric conditions in HVs that were uncovered by objective methods of screening. Physical exam, laboratory testing, toxicology screen and chart review detected conditions that could have a profound influence on volunteer safety, research integrity or both, including severe eating and substance use disorders, recurrent depression, self-injurious behavior, and hepatitis C. Patterns of deception ranged from minimizing symptoms (e.g., case 3) to concealment (e.g., case 1).

As concealment is a characteristic of eating and substance use disorders, they were missed on SCID and psychiatric history. While anorexia nervosa was easy to uncover by obtaining weight and height, the case of hyperkalemia confirms an earlier observation that one screening visit may not be sufficient to detect a psychiatric disorder. For example, Shtasel and colleagues discovered psychiatric disorders after repeated observations of eight volunteers who were admitted to the study as HVs (1). As *hypokalemia* is usually associated with eating disorders, it is not surprising that an eating disorder was not initially suspected. Moreover, psychiatric disorders are a rare and unrecognized cause of hyperkalemia (19, 20).

Although recent drug use can have profound effects on many dependent measures in psychiatry, a toxicology screen is frequently not performed (21). Only 30% of HVs from our sample had a toxicology screen, since it was not required for fMRI studies (17). The prevalence of positive toxicology screens in HVs has been reported between 5.5% (17) and 27.6% (22). Two participants from our sample tested positive for two drugs: cocaine and THC, and cocaine and amphetamine, respectively (17). Drug screens can be falsely positive or falsely negative for various reasons (23–25). Our participant with positive THC probably tried to conceal heavy marijuana use by postponing testing and diluting the urine. Since she tested positive despite urine dilution, her marijuana use was likely higher than she reported. Drug screens may not only detect but also deter some drug users.

Concealment of psychiatric disorders can make participants unduly vulnerable to harm from research (14, 15). When assessing potential harms, additive risks should be considered. For example, although fear conditioning with electric shocks does not pose significant risk in healthy people, it may cause harm in people with severe hypertension, eating disorders, and people using sympathomimetic drugs. While informed consent, exclusion criteria and IRBs play an important role in human subject protection, screening and exclusion of participants with undue risk from research is *sine qua non* for their own safety and the integrity of the research (26). Clinical judgement also plays an important role (26).

“Professional subjects” pose a particular concern for ethics, safety, and research integrity, since, due to financial incentive, they often use deception in order to participate in studies (6, 7, 27). A survey of 100 experienced volunteers found that three-quarters concealed some health information, including participation in another study (43%), health problems (32%), use of prescribed medications (28%), and recreational drugs use (20%) (6). One quarter of volunteers exaggerated their symptoms and 14% fabricated a health condition under study (6). The stylistic and content patterns of deception are summarized in Table 1.

Deception is present in all areas of clinical research (7–12). However, it is a more pronounced problem for psychiatry, which lacks biomarkers and relies on self-reports for diagnosis and treatment response (6, 28). For example, some volunteers simultaneously participate in studies as depressed patients and HVs (28, 29) as there are no objective tests to diagnose depression or to prove mental health. Although there is no data on the prevalence of deception in psychiatric research, its negative impact on research integrity has recently gained more attention (6, 11, 28, 29).

Clinical trials are often done by contract research organizations that, unlike academic institutions that treat patients, rely on volunteers recruited through advertisements (28). Industry-sponsored trials pay investigators by enrolled subjects while screening is inadequately reimbursed, which impacts the quality of enrolled participants (28, 30). In recent years, placebo response rates have increased in major depressive disorder (MDD) trials, with a consequent decrease of treatment effects (31). Increased participation of volunteers who pretend to have depression may contribute to the increasing failure rate in MDD trials (28, 29). Participants who feign depression and then answer truthfully during the medication trial will appear to be responders in both the placebo and the treatment arm, which can reduce statistical power and effect size (32). Failed trials may cause inappropriate discontinuation of the development of potentially effective medications (32).

Detailed eligibility criteria posted on ClinicaTrials.gov may inadvertently facilitate deception if they cannot be objectively verified (6). Moreover, some IRBs require listing of eligibility criteria in informed consents. Overly stringent eligibility criteria may give professional volunteers advantage over appropriate participants (30). Potential harms of deception are shown in Table 2.

Deception is present in all areas of human life. For example, deceptive researchers falsify results to obtain funding or get published (33). Physicians in clinical practice encounter patients with factitious disorders and malingering (34, 35).

Although there are no practical instruments to detect malingering (34) or to flag volunteers who misrepresent their health histories, several strategies to mitigate deception by research volunteers have been proposed (10, 30, 32, 36–38). They are summarized in Table 3. As illustrated by our cases, one of the strategies to mitigate deception among HVs is the use of objective screening methods. While objective methods increase the upfront cost, they are justified if they provide information that is important for participants' safety or study integrity (10).

The purpose of screening of HVs is not to prove health but to determine eligibility for a particular study and exclude participants with conditions that may affect their safety or research integrity. Screening methods should balance study risks, scientific goals, characteristics of the study population (e.g., age), and resources. For some research questions (e.g., feasibility of a new diagnostic interview) histories may be sufficient. For most studies of CNS function involving quantitative objective measure (e.g., fMRI), screening should include some objective methods such as physical exam and a toxicology screen. Psychopharmacology studies usually require laboratory testing ranging from basic tests (e.g., CBC, TSH, chemistries) to comprehensive assessments in investigational drug protocols. Electrocardiograms (ECGs) are appropriate in studies with cardiac risks.

Screening procedures should be carefully chosen since, in addition to costs, there are harms of screening including false positives requiring additional testing, misinterpretation of results, participants' anxiety, labeling, and inappropriate exclusion from other studies (39, 40). For example, although screening ECGs did not detect significant cardiac pathology or affect eligibility for our studies, 22% of young HVs were labelled as having an abnormal or borderline ECG (39). Elevated transaminases due to muscle injury are frequently misinterpreted as liver damage unless creatine kinase is obtained (40).

HVs in psychiatric research are defined by the absence of current psychopathology. Due to different aims, studies exclude or include participants with various degrees of past psychopathology. Variable methods of assessment across studies further contribute to a high heterogeneity of HV samples. While some heterogeneity is justified, there is a need to improve the quality of HV samples by uniform clinical assessments and characterization that, in addition to self-reports and interviews, include objective measures such as physical exam and drug screening. In research institutions, this could be accomplished through centralized recruitment and screening by teams of dedicated clinicians. This may reduce the cost, enhance safety and integrity of psychiatric research and facilitate data sharing.

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References

1. Shtasel DL, Gur Re, Mozley PD, et al. Volunteers for biomedical research. Recruitment and screening of normal controls. *Arch Gen Psychiatry*. 1991; 48(11):1022–1025. [PubMed: 1747017]
2. Schechter D, Singer TM, Kuperman J, Endicott J. Selection of “normal” control subjects for psychiatric research: update on a model for centralized recruitment. *Psychiatry Res*. 1998; 79(2): 175–185. [PubMed: 9705055]

3. Huang DB, Koo H, Dougherty D, Hassan Y. Psychopathology among persons responding to participation as normal controls in behavioral research. *Compr Psychiatry*. 2003; 44(2):83–87. [PubMed: 12658616]
4. Bunce SC, Noblett KL, McCloskey MS, Coccaro EF. High prevalence of personality disorders among healthy volunteers for research: implications for control group bias. *J Psych Res*. 2005; 39(4):421–430.
5. First, MB., Spitzer, RL., Gibbon, M., Williams, JBW. Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Non-Patient Edition. (SCID-I/NP). New York, NY: Biometrics Research, New York State Psychiatric Institute; 2002.
6. Devine EG, Waters ME, Putnam M, et al. Concealment and fabrication by experienced research subjects. *Clin Trials*. 2013; 10(6):935–948. [PubMed: 23867223]
7. Dresser R. Subversive subjects: Rule breaking and deception in clinical trials. *J Law Med Ethics*. 2013; 41(4):829–840. [PubMed: 24446941]
8. Apseloff G, Swayne JK, Gerber N. Medical histories may be unreliable in screening volunteers for clinical trials. *Clin Pharmacol Ther*. 1996; 63(3):353–356.
9. Simmons MS, Nides MA, Rand Cs, Wise RA, Tashkin DP. Unpredictability of deception in compliance with physician-prescribed bronchodilator inhaler use in a clinical trial. *Chest*. 2000; 118(2):290–295. [PubMed: 10936115]
10. Resnik DB, McCann DJ. Deception by research participants. *NEJM*. 2015; 373(13):1192–1193. [PubMed: 26398069]
11. Dickert NW. Concealment and fabrication: The hidden price of payment for research participation. *Clin Trials*. 2013; 10:840–841. [PubMed: 24287132]
12. Council for Clinical Research Subject Safety and Data Integrity. [Accessed April 25, 2017] Pervasive fraud in the clinical trial world. Video. 2010. https://www.youtube.com/watch?v=m_k-ktAgBBU
13. Watson N, Wyld PJ. The importance of general practitioner information in selection of volunteers for clinical trials. *Br J Pharmacol*. 1992; 33(2):197–199.
14. Kolata GB. NIH shaken by death of research volunteer. *Science*. 1980; 209(4455):474–476. [PubMed: 17831358]
15. Darragh A, Kenny M, Lambe R, Brick I. Sudden death of a volunteer. *Lancet*. 1985; 1(325):93–94. [PubMed: 2857036]
16. Gibbons RD, Davis JM, Hedeker DR. A comment on the selection of “healthy controls” for psychiatric experiments. *Arch Gen Psychiatry*. 1990; 47(8):785–786. [PubMed: 1696095]
17. Pavletic AJ, Luckenbaugh DA, Pao M, Pine DS. The importance of medical screening of volunteers participating in research on mental illness. *Prim Psychiatry*. 2008; 15(5):71–76.
18. Mazziotta JC, Woods R, Iacoboni M, et al. The myth of the normal, average human brain - The ICBM experience: (1) Subject screening and eligibility. *Neuroimage*. 2009; 44(3):914–922. [PubMed: 18775497]
19. Pavletic AJ. Hyperkalemia induced by excessive consumption of dried fruits-manifestation of an undiagnosed eating disorder? *Psychosomatics*. 2011; 52(5):494–495. [PubMed: 21907077]
20. Pavletic AJ. An integrated view of potassium homeostasis. *N Engl J Med*. 2015; 373(18):1786–1787.
21. Swerdlow NR, Geyer MA, Perry W, Cadenhead K, Braff DL. Drug screening in “normal controls”. *Biol Psychiatry*. 1995; 38(2):123–124. [PubMed: 7578645]
22. Risch SC, Levine RJ, Jewart RD, Eccard MB, McDaniel JS, Risby ED. Ensuring the normalcy of “normal” volunteers. *Am J Psychiatry*. 1990; 147(5):682–683. [PubMed: 2327510]
23. Moeller KE, Lee KC, Kissack JC. Urine drug screening: Practical guide for clinicians. *Mayo Clin Proc*. 2008; 83(1):66–76. [PubMed: 18174009]
24. Cone EJ, Lange R, Darwin WD. In vivo adulteration: Excess fluid ingestion causes false-negative marijuana and cocaine urine test results. *J Anal Toxicol*. 1998; 22(6):460–473. [PubMed: 9788521]
25. Pavletic AJ, Pao M. Popular dietary supplement causing false positive screen for amphetamines. *Psychosomatics*. 2014; 55(2):206–7. [PubMed: 23932535]

26. Weijer C, Fuks A. The duty to exclude: Excluding people at undue risk from research. *Clin Invest Med*. 1994; 17(2):115–122. [PubMed: 8004847]
27. Tishler CL, Bartholomae S. Repeat participation among normal healthy research volunteers. Professional guinea pigs in clinical trials? *Perspect Biol Med*. 2003; 46(4):508–20. [PubMed: 14593220]
28. Brody B, Leon AC, Kocsis JH. Antidepressant clinical trials and subject recruitment: Just who are symptomatic volunteers? *Am J Psychiatry*. 2011; 168(12):1245–1247. [PubMed: 22193668]
29. Shiovitz TM, Zarrow ME, Shiovitz AM, Bystritsky AM. Failure rate and „professional subjects“ in clinical trials of major depressive disorder. *J Clin Psychiatry*. 2011; 72(9):1284. [PubMed: 21951988]
30. Shiovitz TM, Bain EE, McCann DJ, et al. Mitigating the effects of nonadherence in clinical trials. *J Clin Pharmacol*. 2016; 56(9):1151–1164. [PubMed: 26634893]
31. Khin NA, Chen Y-F, Yang Y, et al. Exploratory analyses of efficacy data from major depressive disorder trials submitted to the US Food and Drug Administration in support of new drug application. *J Clin Psychiatry*. 2011; 72(6):464–472. [PubMed: 21527123]
32. McCann DJ, Petry NM, Bresell A, Isacson E, Wilson E, Alexander RC. Medication nonadherence, “professional subjects” and apparent placebo responders-overlapping challenges for medications development. *J Clin Psychopharmacol*. 2015; 35(5):566–573. [PubMed: 26244381]
33. Hall RI. Mea culpa: Scientific misconduct. *J Cardiothorac Vasc Anesth*. 2012; 26(2):181–185. [PubMed: 22257830]
34. McCullumsmith CB, Ford CV. Simulated Illness: The Factitious Disorders and Malingering. *Psychiatr Clin North Am*. 2011; 34(3):621–641. [PubMed: 21889683]
35. Beach, SR., Taylor, JB., Kontos, N. [Accessed May 2, 2017] Teaching psychiatric trainees to think dirty: Uncovering hidden motivations and deception [published online ahead of print 17 April 2017]. *Psychosomatics*. [http://www.psychosomaticsjournal.com/article/S0033-3182\(17\)30113-5/fulltext](http://www.psychosomaticsjournal.com/article/S0033-3182(17)30113-5/fulltext)
36. Shiovitz TM, Wilcox CS, Gevorgyan L, Shawkat A. CNS sites cooperate to detect duplicate subjects with a clinical trial subject registry. *Innov Clin Neurosci*. 2013; 10(2):17–21. [PubMed: 23556138]
37. Devine EG, Peebles KR, Martini V. Strategies to exclude subjects who conceal and fabricate information when enrolling in clinical trials. *Contemp Clin Trials Commun*. 2017; 5:67–71.
38. Resnik DB, Koski G. A national registry for healthy volunteers in phase 1 clinical trials. *JAMA*. 2011; 305(12):1236–1237. [PubMed: 21406636]
39. Pavletic AJ, Pao M, Pine DS, Luckenbaugh DA, Rosing DR. Screening electrocardiograms in psychiatric research: implications for physicians and healthy volunteers. *Int J Clin Pract*. 2014; 68(1):117–21. [PubMed: 24341305]
40. Pavletic AJ, Pao M, Wright ME. Exercise - induced elevation of liver enzymes in a healthy female research volunteer. *Psychosomatics*. 2015; 56(5):204–5.

Table 1

Patterns of deception by research volunteers

Minimizing or concealing psychiatric and medical conditions or symptoms
Minimizing or concealing alcohol, drug and tobacco use
Concealing over the counter and prescription medication use
Concealing simultaneous and sequential participation in multiple trials
Repeat participation in the same study (multisites studies)
Concealing research related radiation exposure
Dilution and adulteration of urine sample
Nonadherence with study procedures or medications
Exaggeration of symptoms
Pretending to have condition under study
Underreporting of side effects

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Table 2

Potential harms of deception

Research participants
Adverse events due to preexisting conditions or drug-drug interaction
Adverse events due to overenrollement in phase 1 clinical trials
Anemia due to excessive blood draws for multiple studies
Increased risk for cancer due to excessive radiation exposure
Research study
Compromized data integrity
Failed medication trial due to increased placebo effect
Side effects falsely attributed to study drug
Side effects of study drug not recognized
Research in general
Compromized safety and integrity
Compromized reputation
Increased cost
Discontinuation of the development of effective medications
Society
Scepticism about safety and integrity of clinical research
Scepticism about efficacy of psychiatric medications
Patients deprived of potentially effective medications
Delayed delivery of new medications

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Table 3

Strategies to mitigate deception

Advertising (e.g., omission of payment information and detailed exclusion criteria) (37)
Payment (e.g., withholding payment for volunteers who conceal drug use) (37)
Telephone screening (e.g., non-leading questions) (37)
In person screening (objective methods, e.g., physical exam, drug screen) (10, 37)
Observing of subjects' behavior (e.g., preoccupation with payment schedule) (37)
Attending to inconsistencies in participants' history (37)
Utilization of outside source (e. g., medical records) to confirm history (30)
Reinforcements to promote truthfulness (10, 32)
Biomarker or medication adherence technology (30, 32)
Establishment and utilization of participant registries (30, 36, 37)
Establishment of national registry for healthy volunteers in phase 1 clinical trials (38)

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