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Substance use onset in high-risk 9–13 year-olds in the ABCD study

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Abstract

Aim: A key aim of the Adolescent Brain Cognitive Development℠ (ABCD) Study is to document substance use onset, patterns, and sequelae across adolescent development. However, substance use misreporting can obscure accurate drug use characterization. Hair toxicology provides objective historical substance use data but is rarely used in studies of youth. Here, we compare objective hair toxicology results with self-reported substance use in high-risk youth.

Methods: A literature-based substance use risk algorithm prioritized 696 ABCD Study® hair samples from 677 participants for analysis at baseline, and 1 and 2-year follow-ups (spanning ages 9–13). Chi-square and *t*-tests assessed differences between participants' demographics, positive and negative hair tests, risk-for-use algorithm scores, and self-reported substance use.

Results: Hair testing confirmed that 17% of at-risk 9–13 year-olds hair samples had evidence of past 3-month use of one ($n = 97$), two ($n = 14$), three ($n = 2$), or four (n = 2) drug classes. After considering prescribed medication and self-reported substance use, 10% had a positive test indicating substance use that was not reported. Participants with any positive hair result reported less sipping of alcohol ($p < 0.001$) and scored higher on the risk-for-use algorithm ($p < 0.001$) than those with negative toxicology results.

Conclusions: 10% of hair samples from at-risk 9–13 year-olds tested positive for at least one *unreported* substance, suggesting underreporting in high-risk youth when participating in a research study. As hair testing prioritized youth with risk characteristics, the overall extent of underreporting will be calculated in future studies. Nonetheless, hair toxicology was key to characterizing substance use in high-risk youth.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ntt.2022.107090.

Keywords

Children; Adolescents; Hair toxicology; Substance use; Substance use onset; Self-report; Hair samples

1. Introduction

The Adolescent Brain Cognitive Development℠ (ABCD) Study is a landmark project of healthy development following primarily substance-naïve youth (9–10 years-old) prospectively for 10 years with the expectation that a proportion will initiate substance use (Lisdahl et al., 2018). The neurocognitive, psychosocial, psychiatric, and neurobiological predictors and sequelae of substance use are evaluated. The ABCD Study® employs the Timeline Follow-Back (Sobell and Sobell, 1992) gold standard for reporting substance use, a self-report semistructured interview where participants are guided to recall their past year's substance use patterns including dose, estimated potency, and routes of administration (Lisdahl et al., 2018).

Retrospective self-report has limitations. Lack of accuracy, regardless of participant age, may be due to intentional or unintentional misreporting, due to perceived desirability, concerns regarding privacy (Johnson, 2014; Williams and Nowatzki, 2005), forgetting, and lack of knowledge of substances taken (Johnson, 2014). Some factors influencing reporting accuracy include demographics (Livingston and Callinan, 2015), mental health (Harris et al., 2008), age of first use (Harris et al., 2008), frequency of use (Livingston and Callinan, 2015), and guidance regarding standard units (Gilligan et al., 2019). Age may also influence substance use disclosures, though this was not investigated and the accuracy of adolescents' self-reported substance use is not well understood. Many prior youth studies were conducted in treatment or juvenile detention facilities or as part of a community-based substance use study, settings carrying differential motivation to misrepresent their use. One study of a generally healthy population of male adolescents whose fathers had alcohol dependence revealed a 13% discordance rate between adolescent self-report and urine drug screen results (Williams and Nowatzki, 2005). Others have used hair to detect additional alcohol and nicotine use than reported in adolescents (Bertol et al., 2017). Recently, advanced analyses utilizing data on misreporting estimated that self-reported cannabis use in Washington State adolescents is underreported, with 7% who took cannabis in the past month denying use (Murphy and Rosenman, 2019). A larger characterization of self-report accuracy in relation to objective substance use measures is important, particularly in adolescents.

Though the Timeline Followback was validated with test-retest assessment and toxicology in adults (Crunelle et al., 2014; Hjorthoj et al., 2012; Smith et al., 2018), a new gold standard of combining self-report with objective measurement was proposed (Smith et al., 2018). Accordingly, the ABCD Study was designed to measure substance use with both self-report and multiple toxicological measurements. Consistent with project goals, the vast majority of ABCD participants self-reported being substance naïve at baseline, except for caffeine (Lisdahl et al., 2021). Recent (24 h) substance use is assessed with breathalyzer for alcohol, urinalysis for nicotine, and oral fluid for other drugs (Lisdahl et al., 2018; Uban et al., 2018).

To detect substance use in the past 3 months, hair samples were collected and analyzed (Taylor et al., 2017).

Hair testing measures specific drug analytes (e.g., cannabidiol, or CBD; Δ-9-tetrahydrocannabinol, or THC; (Citti et al., 2018)). Hair collection is (1) non-invasive (unlike blood), (2) not limited to recent consumption (unlike oral fluid or blood), (3) less susceptible to adulteration or dilution (unlike urine), (4) and suggests intensity of substance use (Berthet et al., 2016; Huestis and Smith, 2018). On average, drug analytes and metabolites are incorporated into the hair immediately, but the hair with the incorporated drugs does not emerge from the scalp until about 8 days since last use (Scheidweiler et al., 2005; Polettini et al., 2012). Importantly, while highly specific, hair analyses may not detect low levels (e.g., sipping, puffing) of substance use (Kintz, 2019), and some substances (e.g., alcohol) require closer to moderate levels of use for detection (Boscolo-Berto et al., 2014). Damaged or chemically-treated hair may have lower analyte concentrations, and must be considered for proper interpretation (Cuypers and Flanagan, 2018). Environmental exposure from smoke, dust, or transfer from hands can also increase analyte concentrations, increasing the risk of false positives, though proper hair wash procedures can mitigate this risk, including removing contamination from secondhand smoke (Cuypers and Flanagan, 2018; Hill et al., 2016). Mass spectrometric screening and/or confirmation of drug analytes provides high sensitivity and specificity for hair test results (Cooper et al., 2012; Leghissa et al., 2018).

One ABCD Study challenge is balancing study needs with participant burden and financial constraints. Toxicological assessment ranges from multiple dollars to over $200 per sample, making it cost prohibitive to test all 11,878 ABCD participants' samples with all forms of measurement annually. Early in the ABCD study, a small percentage of participants were randomly assigned to testing with oral fluid, breathalyzer, or nicotine urine tests. Although hair was collected from 70% of participants and stored for future analysis, 696 samples from 677 participants (i.e., 19 participants with two tested samples from different time points) were selected for hair analysis based on an expert-devised evidence-based algorithm prioritizing samples according to known risk factors for substance use onset. In addition, participants who self-reported substance intake received toxicological testing during their session(s) and, as financially permissible and warranted based on the risk algorithm, by hair analysis.

We present initial ABCD cohort toxicological outcomes from findings in annual release 3.0 of the ABCD Study, consisting of baseline (9–10-year-olds), one-year (10–11-year-olds), and two-year (11–12-year-olds) data. First, we present basic descriptive toxicological and demographic information from a subsample at risk for early substance use. In this subsample, we investigated discrepancies between self-report and toxicological hair findings. Given data suggesting that adolescents underreport substance use, we hypothesized that hair analysis would identify additional substance exposure compared to self-report alone. Finally, we expected that participants who had positive hair tests would have higher scores on the risk-for-use algorithm.

2. Material and methods

2.1. Participants

The ABCD Study is a 21-site longitudinal study of 11,878 participants funded by the National Institutes of Health and partner institutes. Participants were recruited predominately through school-based recruitment guided by epidemiological data (Garavan et al., 2018). The ABCD Study NDA 3.0 data release (Consortium, A.B.C.D.S, 2020) includes hair toxicology results for 696 samples from 677 participants, and self- and parent substance use reports at the baseline, 1-year follow-up, and 2-year follow-up time points (i.e., ages ranging from 9 to 13 years).

2.2. Measures

2.2.1. Demographics—Participants and their parents reported demographic characteristics, including the child's sex at birth, household annual income, highest parental education, parent marital status, and race/ethnicity (Barch et al., 2018). Some variables are social constructs requiring careful contextualization (Simmons et al., 2021), limiting interpretability of these factors in this small subsample.

2.2.2. Acute on-site multi-matrix toxicological testing—Acute toxicological assessment was performed on approximately 10% of randomly selected youth as well as those who reported any past-year substance use. This testing included: (1) the Dräger Drug Test® 5000 (DT5000; Dräger Inc., Houston, TX) oral fluid test consisting of a 7-panel screen for cocaine, opiates, cannabis, benzodiazepines, amphetamine, methamphetamine, and methadone; (2) a breathalyzer test for ethanol; and (3) NicAlert strips (JANT Pharmacal, Encino, CA) for urinary cotinine; to assess for past 12–72 h substance exposure.

2.2.3. Youth substance use interview—Youth participants completed a research assistant (RA)-administered substance use interview (Lisdahl et al., 2018). Youth were first reminded of confidentiality and asked if they had "heard of" a list of substances. If a participant had not heard of a substance, they were not asked about its use; otherwise, participants were asked about use of each major drug category, including low level use such as alcohol sipping or nicotine/cannabis puffs/tastes. Participants endorsing past-year substance use completed a detailed 12-month Timeline Followback interview about alcohol, nicotine (cigarettes, electronic nicotine delivery systems, smokeless tobacco, cigars, hookah, pipe, and nicotine replacement products), cannabis (smoked/vaped flower, smoked blunts, edibles, smoked/vaped concentrates, oral tinctures, and cannabis-infused alcohol drinks, synthetic cannabinoids), cocaine, cathinones, methamphetamine, ecstasy/MDMA, ketamine, gamma-hydroxy-butyrate, heroin, hallucinogens, psilocybin, salvia, anabolic steroids, inhalants, prescription stimulants, sedatives, and opioid pain relievers, and over the counter (OTC) cough/cold medicine use. Full reporting of substance use from ABCD's cohort at baseline can be found in Lisdahl et al. (Lisdahl et al., 2021).

2.2.4. Peer and familial substance use measures—Youth reported the number of their peers who used cannabis (Johnston et al., 2015). The Family History Assessment Module Screener (FHAM-S; (Rice et al., 1995)) assessed drug or alcohol use problems

of any biological family member of the youth, as reported by the parent/guardian. Parents/guardians completed the Adult Self Report (Achenbach, 2009), including 3 items on parent substance use (drinking too much, daily cigarette use, and illicit substance use).

2.2.5. Childhood behavior checklist (CBCL)—The CBCL (Achenbach, 2009) contains questions about youths' behavioral and mental health; it is completed by the parent/guardian. Normed externalizing symptoms (e.g., behavioral or social disturbances) were calculated.

2.3. Procedures

Participants were assessed by trained RAs at each of the 21 ABCD research sites. Parents provided written informed consent, while youth assented. Youth participated with one parent/guardian at baseline and year 2 follow-up for approximately seven hours of behavioral, neuroimaging, and biological assessment over one or two sessions. At year 1 follow-up, the visit was typically 3 h. Parents and youth took part separately in the protocol, with all aspects approved by a centralized Institutional Review Board.

Hair samples were collected by RAs according to standardized procedures and stored for each participant who agreed to collection and had any head hair longer than 1 cm. RAs noted hair length and color, and hair damage or dyeing. All samples were securely stored in temperature-controlled rooms and locked cabinets at the data collection site. Samples were collected from approximately 70% of participants each year; however, the cost of analyzing the samples is high and was not possible for all samples, requiring the use of a Hair Test Risk Algorithm (see below). Selected hair samples were shipped to Psychemedics (Culver City, CA). After receipt, hair was trimmed to 3.9 cm from the root, providing an average window of substance use detection of 3-months. Hair was enzymatically digested by a patented procedure (Hill, 2013) and each drug class was separately screened by FDA-cleared immune-assays or by Laboratory Developed Tests via LC-MS/MS (for Δ-9-tetrahydrocannabinol [THC], Δ9-tetrahydrocannabivarin [THCV], cannabidiol [CBD], cannabinol [CBN], and ethyl glucuronide [EtG]). Samples then underwent a 15-min wash procedure with 2 mL isopropanol per 12 mg hair, followed by three 30-min phosphate buffer washes and, for most drugs, an additional two 60-min phosphate buffer washes (Hill et al., 2016). This reduced possible false-positive test results from exposure via external contact only, as hair washing removes most environmental drug residue. In addition, in initial methods validations, Psychemedics tested over 70 compounds for interference, with no interference found. Each presumptive positive sample was confirmed and quantified by LC-MS/MS or GC–MS/MS analysis (Hill et al., 2016; Hill et al., 2014). Samples were tested to the limit of detection (e.g., for THCCOOH, 0.02 pg/mg) to maximize sensitivity (see Table 1) due to the low expected degree of exposure in this young cohort.

An adequate hair sample was 100 mg (typically 3.9 cm in length) to complete all screening and confirmatory analyses. For some samples with insufficient weight/mass, testing was performed for as many analytes as possible, with untested screening or confirmation analyte results labeled "Quantity Not Sufficient" (QNS). Tested drug classes included cocaine, opioids, phencyclidine, amphetamines, cannabinoids, alcohol, nicotine, fentanyl,

and benzodiazepines. Other analytes were available as follow-up for some samples, hence fewer results were reported for these analytes (e.g., meta-hydroxycocaine).

Biannually, the Data Analytics, Informatics, and Resource Center (DAIRC) of the ABCD Study calculates the hair test risk score for each participant with hair samples available. Samples from those with higher scores on the algorithm, more recent hair collections, participants who previously tested positive, and participants who tested positive on acute toxicological assessment are prioritized. Data collection sites are requested to ship the selected samples to the Psychemedics laboratory for analysis. Psychemedics analyzes the samples as described above, with screen, confirmation, and quantified analyte results provided to the DAIRC for upload to the NDA data release.

2.3.1. Hair test risk algorithm—As noted above, a significant challenge for toxicology testing in the ABCD Study is the cost to test each participant's sample. Thus, members of the ABCD Substance Use Work Group (including SFT, KML, FH) and an outside consultant toxicology expert (MAH) used the existing substance use risk literature to devise an algorithm to prioritize analysis of samples for those most likely to have substance. This approach relied on prior studies (e.g., (Gorka et al., 2014; Heron et al., 2013; Maggs et al., 2015)) and reviews (e.g., (Clark and Winters, 2002; Donovan and Molina, 2011)) of risk factors in youth who transition to substance use. The algorithm includes any use of cannabis, tobacco, prescription medications for non-medical purposes, cannabidiol (CBD), any positive oral fluid or breathalyzer test; youth reporting curiosity about trying cannabis, peer cannabis use, or youth reporting they will try cannabis soon; externalizing symptoms (reported on the Child Behavior Checklist), parental self-report of drug use or drinking too much alcohol, parental self-reported amount of tobacco used per day, any biological family member with drug use problems, any biological family member with alcohol use problems, youth reported drinking without parents' approval, age and prior positive hair tests.

Initial algorithm weighting was determined to detect any substance use in the highest risk participants (e.g., 3 point scored per substance use reported). Additional weighting was added to variables that were specific to overarching ABCD study aims (e.g., the aim of identifying cannabis use onset and its sequelae; any cannabis use was scored as 10 points). As it is anticipated that more participants will use substances as they get older, more recent ABCD timepoints were also prioritized through up to an additional 2 point boost in scoring. In addition, participants with prior positive hair toxicology results and positive acute toxicology tests were prioritized through receiving an automatic maximum score. Variables collected in the ABCD Study populated the algorithm (see Supplemental Table 1 and https://osf.io/mtp4k/ for full list and scores).

2.4. Statistical analysis

SPSS 26 was utilized for all statistical analyses. Demographics (mean, SD, range, or percentage) were examined for the whole sample and by each positive substance. Both initial hair screening results as well as hair confirmation results are reported. Demographic and self-reported substance use group differences between those with positive confirmed hair toxicology results and those with negative results were assessed with chi-square and

t-tests. While these analyses include assessment for differences in race/ethnicity, we note that race/ethnicity itself is a proxy for a number of different variables (e.g., educational opportunities; socioeconomic status; acculturation (Manly, 2006)); thus, race/ethnicity findings are reported but not discussed. As differences in demographics and potential risk behaviors (i.e., alcohol sipping) were noted between participants with positive and negative results, a regression was run to determine whether the alcohol sipping results persisted even after controlling for demographics factors. Finally, a *t*-test was run to evaluate differences in hair risk score between those with positive and negative hair toxicology results. As 19 participants had hair samples tested from two separate annual study time points, results were run both including all samples ($n = 696$) and without participants whose hair had been assayed on two occasions ($n = 658$); results remained the same in either case, with results from all available samples presented here.

3. Results

3.1. Descriptive data

3.1.1. Demographics—Hair analysis was performed on 696 samples, including two samples for each of 19 participants. Mean ± SD participant age at time of sample collection was 10.65 ± 1.02 years (9–13.3), with 47.1% ($n = 328$) from females. Full demographic details are presented in Table 2, with 61.4% Baseline samples, 16.9% Year 1 Follow-Up, and 21.8% Year 2 Follow-Up. No participants reported using substances recreationally at a level that should produce positive hair tests at the same annual time point.

3.1.2. Hair toxicology results—Positive screening results were obtained for 131 of 696 hair samples, with ten samples not confirming and five samples having an insufficient amount of hair for confirmation, yielding 116 hair samples that were confirmed positive. Of these, 97 were positive for one, 14 for two, two for three drug classes and two for four drug classes. Frequency of positive results by drug class by screening results and confirmation results are reported in Table 3.

3.1.3. Group differences between positive and negative hair samples—Participant characteristics from hair samples with positive tests included being more likely to be male ($\chi^2 = 5.65$, df = 1, $p = 0.02$, d = 0.18), have less educated parents ($\chi^2 = 37.71$, df = 4, $p < 0.001$, $v = 0.11$), lower income ($\chi^2 = 26.93$, df = 2, $p < 0.001$, $v = 0.14$), be black ($\chi^2 = 20.05$, df = 4, $p < 0.001$, $v = 0.08$), and have unmarried parents ($\chi^2 = 18.49$, df = 1, $p < 0.001$, d = 0.33). Positive hair samples (POS) did not differ by age of participant at time of sample collection or assessment time point from those with negative hair samples (NEG). In assessing alcohol sipping behavior, NEG were significantly more likely than POS to have participant-reported sipping alcohol at that study time point ($\chi^2 = 16.63$, df = 1, $p < 0.001$, d = 0.31), even after controlling for demographic differences as listed above ($\beta = 0.149$, $t_{649} = 2.92$, $p = 0.004$). In contrast, POS and NEG group members did not differ in self-reported low-level nicotine (cigarette or ENDS) ($\chi^2 = 2.54$, df = 1, $p = 0.11$, d = 0.12) or cannabis use ($\chi^2 = 1.46$, df = 1, $p = 0.23$, d = 0.09). At study visits with POS samples, 11.2% ($n = 13$) of participants reported using any drug as more than a sip or puff, compared to 10.2% ($n = 59$) of NEG ($p = 0.74$).

3.1.4. Hair toxicology relative to self-reported prescription/OTC medication use—We evaluated the data for reported prescription or OTC medications that may explain positive toxicology results; 64 participants with positive hair tests also self-reported recent prescription or OTC medication use (primarily amphetamine or methylphenidate) at that study visit. For positive amphetamines tests, 47 of 58 (81%) self-reported prescriptions, accounting for their positive amphetamine findings. An additional eight participants prescribed amphetamine or methylphenidate were *not* positive for amphetamines in hair. No other reported medications explained any positive result. Seventy-two of 696 (10.3%) of participants' hair samples identified substance exposure unexplained by self-reported prescription or OTC medication use.

3.1.5. Hair toxicology relative to other toxicology results and self-report—All 116 samples with positive results were assessed for other toxicology and self-report data occurring at the same study time point. Full results by drug analyte are available in Table 4. Overall, 51.7% of participants with positive hair results reported some level of substance use at that study visit, including experimentation through puffing nicotine or cannabis or sipping alcohol (which is too low a dose to be detected by hair analysis; e.g., 47% of the sample reported alcohol sipping). In those who had positive hair results, 11% reported use of a full standard consumption unit (e.g., 12 oz of a beer) of a substance, while 10% of those who had positive tests reported a full unit of substance use. In positive-hair result samples (n = 116), only three reported use of the substance for which they tested positive at that study time point. Of these three, one reported use only occurred once and was nearly a year prior to sample collection. Nine of the 13 participants reported use outside the 3-month window of detection from the hair sample. Irrespective of the window of detection, 69 of 696 samples (10%) contained positive results indicating a substance was used (beyond puffing or sipping) that would not have been known without hair analysis. When comparing hair results to self-report, there was no difference in self-reported substance use rates between POS and NEG samples ($\chi^2 = 0.112$, df = 1, $p = 0.74$).

Within participants with positive hair toxicology results at the corresponding study visit, full standard units of substances reported were alcohol (n = 1), nicotine (n = 5), cannabis (n = 3), inhalants (n = 1), and non-prescribed amphetamines (n = 1). Forty-three POS also had oral fluid test results at that same study time point, though no participants were positive for any non-prescribed medications or drugs. Six participants with positive hair samples had urinary cotinine testing during the same study visit, with one participant's urinary cotinine level indicating recent nicotine use. Nineteen POS underwent breathalyzer testing and no participants had a breath alcohol level above 0.000.

3.1.6. Hair test risk algorithm—A t-test assessed group differences in the hair test risk algorithm score by confirmed hair results. Participants with positive hair results had significantly higher risk algorithm scores at the study visit when hair collection occurred ($t_{694} = 6.33$, $p < 0.001$, d = 0.58). Further, we analyzed whether, within participants with positive hair results, scores were higher in participants who also reported at least one standard unit of any substance. Participants who did *not* report any substance use at the same

study visit as hair was tested had marginally significantly higher hair test risk algorithm scores than those who did report substance use ($t_{114} = -1.769$, $p = 0.08$, d = 0.62).

4. Discussion

Self-report of substance use can be limited by intentional and unintentional misreporting. This may be even more the case in youth engaged in a healthy development study, though accuracy of report is understudied in adolescence and, particularly, pre-adolescence. This novel investigation assessed substance use self-report in high-risk youth and objective hair toxicology analysis that permits a larger 3-month substance use history window. Primarily, our findings show that 10% of youth in this high-risk sample are exposed to substances that they are not reporting. Given use of a wash procedure to greatly reduce environmental (including secondhand) exposure and mass spectrometric confirmation of all drug-positive results, it is likely that exposure is through personal substance use. Youth could also be timing their use to be outside the detection window for acute toxicology assessments. Second, participants with a positive hair toxicology result had a higher score on the evidence-based risk algorithm; though positive participants who denied any substance use had a trend toward higher hair test algorithm scores. On balance, given this was a carefully curated algorithm and thus a non-random, high-risk sample, the general prevalence of actual substance use among 9–13 year-olds is still uncertain, indicating greater toxicology testing of hair is needed both within the ABCD Study sample and in substance use research more broadly.

Results suggest that a small percentage of high-risk youths are likely using substances that are detectable on highly specific hair analyses but denying it when queried. Even in youth who report some low-level substance use (e.g., alcohol sipping or nicotine puffing), based on their hair results, some participants appear to minimize self-reported use. Several dozen participants reported substance use levels as more than a sip or puff at baseline (ages 9–10), suggesting not all youth deny substance use on interview (Lisdahl et al., 2021). It is important to note that hair toxicology may not detect low level substance use (Taylor et al., 2017), though detection of even single use occasions is possible (Kintz, 2019) and measurement was assessed at the limit of detection to maximize sensitivity. Also, some youth may unknowingly consume a substance (e.g., believe they are vaping flavoring rather than nicotine, or smoke cannabis laced with a novel psychoactive substance) and thus unintentionally misreport their use. Toxicology tests, and specifically hair tests with their much longer window of drug detection, provide the best means of capturing substance use onset. While results here suggest that the current hair selection algorithm for targeted testing of high-risk youth is useful, this does not guarantee that other ABCD youth have not also started using substances; nor are results representative of the full, generally healthy sample, as participants were not randomly selected for testing. Future years of ABCD data collection plan to broaden acute drug screens to all participants and analyze a larger subset of hair samples from participants, including participants randomly selected without regard to their hair risk score. Such expanded testing will better detail the effects of the onset of substance use and the general rate of substance use in a healthy development study.

Interestingly, several risk factors for early substance use onset were more commonly identified in these high risk youth whose hair tested positive: being male (Donovan, 2007) and of lower socioeconomic status (Shah and Watson, 2020). Greater rates of male substance use is also consistent with the broader ABCD cohort, where males report higher levels of early substance experimentation (e.g., sipping, puffing) than females (Lisdahl et al., 2021). Further, scores on the evidence-based algorithm developed to identify early onset based on common risk factors were significantly higher in individuals with positive hair results. This may be encouraging, as it further indicates that the field accurately identified risk factors for substance initiation that may be useful for preventive efforts. Importantly, as only two participants tested positive for a substance and reported use of that substance in the same 3-month window, results may also reflect characteristics of those who use substances but deny it on interview. Interestingly, another common risk factor, reporting early alcohol sipping, was *not* related to positive hair toxicology results. It is unclear whether this is due to early experimenters, but not frequent users, having less concerns regarding privacy, or due to the fairly common nature of sipping (Lisdahl et al., 2021; Watts et al., 2020), or some other factor. Together this suggests further refinement of the most salient risk factors in pre-adolescent youth are needed. As the ABCD study is still in its early stages and youth are just entering the time of predicted early substance use onset, it will be important to carefully follow these selected youth, as well as the rest of the cohort, over time.

Hair samples are beneficial for confirming substance exposure over long periods of time. However, hair cannot reveal date of last use, nor does it suggest the exact product used (e.g., cannabis flower v. dabs), route of administration (e.g., vaping v. smoking), frequency of use, co- or simultaneous-use, or other patterns (e.g., weekday v. weekend use). Importantly, use of hair samples does not negate the need for collection of other metrics, including self-report. Low levels of use (e.g., sipping or puffing) are not expected to be detected, and thus require relying on participant-reported substance use information. Further, as it can take up to eight days for the hair with incorporated drug analytes to emerge from the scalp for hair collection drug analytes (Scheidweiler et al., 2005; Polettini et al., 2012), self-report and other bioassays (e.g., urine, oral fluid) are necessary to assess for past-week substance use. Environmental factors (e.g., parental smoke) should also be considered as potential means of contaminating hair samples, though use of hair washing protocols should significantly lessen this risk (Cuypers and Flanagan, 2018; Hill et al., 2016). Such factors are likely key to understanding the full impact of substance initiation on cognitive and other outcomes, and so it is important to collect self-report and objective substance measurement whenever possible. Hair samples also were correlated with self-reported use, urine, and oral fluid tests in another study (Meersseman et al., 2016).

4.1. Study limitations

Together, findings from the present analyses suggest robust, objective measurement of substance use is needed to ensure accuracy of self-report of substance initiation. However, these results are not without limitations. First, hair toxicology analyses may not be sensitive to low levels of substance use despite the low limits of detection in this study (Table 1). In addition, hair samples may not identify early experimentation of use, as a minimal detectable dosage is not established for some drugs of abuse (Kintz, 2019). Though an

extensive hair wash procedure was employed (Hill et al., 2016), there is the possibility of environmental drug exposure. Hair samples are also limited to the length of hair analyzed. Thus, as all hair sampled in the present study was trimmed to 3.9 cm, results reflect only the past three months of substance use. In contrast, past year history of substance use was queried, which prevents full assessment of congruent reporting. Certain youth may be more likely to decline or be unable to contribute hair samples (e.g., those with short hair "fades", braids, or dreadlocks). In addition, there were a number of samples that did not have sufficient quantity of hair (QNS) for analysis, including five who screened positive but whose results were unable to be confirmed, suggesting we could underestimate the total number of positive results. Finally, given the financial cost of hair analyses, samples selected were restricted to those most likely to be underreporting substance use. For this reason, findings are not generalizable to the general population, or even to the overall ABCD cohort. More broad-based, randomized hair sampling is needed to better understand prevalence of underreporting in healthy developing youth.

In summary, initial hair toxicology results from the ABCD cohort suggest that a small percentage of 9–13 year-olds identified as most likely to initiate substance use may underreport substance use. We found 10% of high-risk youth with assayed samples positive for at least one substance that was not otherwise reported, with some participants using three or more drug classes, including alcohol, nicotine, cannabis, and cocaine, although few self-reported even minimal use. Thus, to accurately determine the consequences of substance use in youth, greater use of robust hair samples is needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Limits of detection for each drug analyte.

Drug class	Analyte	Level of detection
Cocaine	Cocaine	0.025 ng/mg
	Benzoylecgonine	0.025 ng/mg
	Cocaethylene	0.025 ng/mg
	Norcocaine	0.025 ng/mg
	Metahydroxycocaine	0.4 pg/mg
	Orthohydroxycocaine	0.4 pg/mg
	Parahydroxycocaine	0.4 pg/mg
Opiates	Codeine	0.05 ng/mg
	Morphine	0.025 ng/mg
	6-Acetylmorphine	0.025 ng/mg
	Oxycodone	0.05 ng/mg
	Oxymorphone	0.05 ng/mg
	Hydrocodone	0.05 ng/mg
	Hydromorphone	0.05 ng/mg
PCP	Phencyclidine	0.10 ng/mg
Amphetamines	Amphetamine	0.025 ng/mg
	Methamphetamine	0.025 ng/mg
	MDA	0.025 ng/mg
	MDMA	0.025 ng/mg
	MDEA	0.025 ng/mg
Nicotine	Cotinine	10 pg/mg
Natural Cannabinoids	THC	5 pg/mg
	CBN	5 pg/mg
	CBD	5 pg/mg
	THCV	5 pg/mg
THCCOOH	Carboxy-THC	0.02 pg/mg
Alcohol	Ethyl Glucuronide	1.0 pg/mg
Benzodiazepines	Temazepam	5 pg/mg
	Phenazepam	5 pg/mg
	Oxazepam	5 pg/mg
	Nordiazepam	5 pg/mg
	Midazolam	5 pg/mg
	Lorazepam	5 pg/mg
	Flunitrazepam	5 pg/mg
	Diazepam	5 pg/mg
	Clonazepam	5 pg/mg
	Alprazolam	5 pg/mg

Table 2

Demographics of ABCD participants with hair toxicology tests, and those with positive and negative hair test results indicating substance exposure.

	Hair toxicology subsample	Confirmed positive via hair	Confirmed negative via hair	Significant difference by confirmed result
	(n = 696)	**(n = 116)**	**(*n* = 580)**	
Age (years; range: 9–13)	10.65 years (SD = 1.02)	10.8 (SD = 1.00)	10.62 (SD = 1.02)	–
Female	47.1%	37.1%	49.1%	$p = 0.02$
Parents married	63.1%	45.7%	66.6%	$p < 0.001$
Race/ethnicity				$p < 0.001$
Asian	0.7%	0%	0.8%	
Black	5.3%	12.9%	3.8%	
Hispanic	17.8%	17.2%	17.9%	
White	64.4%	54.3%	66.4%	
Other/multiple	11.8%	16.4%	11.0%	
Parent education				$p < 0.001$
Less than high school diploma	3.1%	6.9%	2.4%	
High school/GED	7.6%	13.8%	6.4%	
Some college	29.0%	43.1%	26.2%	
Bachelor's degree	27.3%	12.1%	30.3%	
Post graduate degree	32.9%	24.1%	34.7%	
Yearly household income				$p < 0.001$
<$50,000	26.0%	44.8%	22.2%	
≧$50,000 and <$100,000	27.4%	20.7%	28.8%	
≧$100,000	40.2%	27.6%	42.7%	
Time point				–
Baseline	61.4%	56.0%	62.2%	
Year 1 follow-up	16.9%	21.5%	16.0%	
Year 2 follow-up	21.8%	22.4%	21.7%	

Notes: If a significant difference ($p < 0.05$) was found for those with positive and negative hair tests, the p value is listed; sum totals of categories which are less than 100% are due to participants reporting "Don't Know" or "Refuse to Answer"; sample size is calculated from the total number of hair samples assayed, with participants whose hair was assayed at two time points counted individually.

Table 3

Frequency of screening and confirmation positives by drug class.

	Positive screening results (*N* = 128)	% of sample	Positive confirmation results (N = 116)	% of sample
Cocaine	13	1.9%	13	1.9%
Opiates	2	0.3%	2	0.3%
PCP	0	0%	–	–
Amphetamines	64	9.2%	59	8.5%
THCCOOH	25	3.6%	25	3.6%
Natural cannabinoids	25	3.6%	22	3%
Cannabis (either)[a]	41	5.9%	37	5.3%
Ethyl glucuronide	11	1.6%	9	1.3%
Cotinine	28	4%	19	2.7%
Benzodiazepines	0	0%	–	–
Fentanyl	0	0%	–	–

Notes: Frequency of each drug class is reported; % of Sample refers to the total number of hair samples available (n = 696); 53 participants whose hair was positive for amphetamines also reported having a prescription for amphetamines; 11-nor-9-carboxy-tetrahydrocannabinol (THCCOOH) is a Δ9-tetrahydrocannabinol (THC) metabolite; Natural cannabinoids refers to phytocannabinoids (THC, cannabidiol (CBD), cannabinol (CBN), or Δ9-tetrahydrocannabivarin (THCV); no drug class is mutually exclusive; PCP phencyclidine, ETG ethyl glucuronide.

[a]Cannabinoids (either) indicates a hair sample that is positive for either THCCOOH or Natural Cannabinoids or both.

Table 4

Positive acute toxicology results and self-reported use endorsements for participants with confirmed positive hair results, by drug class.

	Cocaine	Opiates	Amphetamines	THCCOOH	Natural cannabinoids	Alcohol	Nicotine
	(n = 13)	(n = 2)	(n = 59)	(*n* = 25)	(*n* = 22)	(n = 9)	(*n* = 19)
Self-reported use:							
Alcohol sips	38.5%	50%	40.7%	48.0%	59.1%	66.7%	52.6%
Alcohol full drink	0%	0%	0	4.0%	4.5%	0%	0%
Nicotine puffs	15.4%	50%	5.1%	16.0%	22.7%	11.1%	21.1%
Nicotine more than puff	7.7%	0%	0%	4.0%	4.5%	11.1%	5.3%
Cannabis puff	7.7%	50%	0%	12.0%	9.1%	11.1%	10.5%
Cannabis more than puff	7.7%	50%	0%	4.0%	4.5%	11.1%	5.3%
Other drugs	0%	0%	2%	0%	0%	0%	5%
Hair analyte confirmation[b]							
Cocaine[d]	13/13						
Benzoylecgonine	12/12						
Norcocaine	2/11						
Oxymorphone[c]		2/2					
Amphetamines[e]			52/59				
Methamphetamine			9/51				
THCCOOH				25/25	10/11		
THC				9/10	21/22		
CBN				3/5	5/7		
CBD				5/5	8/11		
THCV				0/2	0/4		
ETG						9/9	
Cotinine							18/19
3-Hydroxycotinne							6/11
Norcotinine							1/1
Nornicotine							8/8
Draeger oral fluid test[f]							

	Cocaine	Opiates	Amphetamines	THCCOOH	Natural cannabinoids	Alcohol	Nicotine
	(n = 13)	**(n = 2)**	**(n = 59)**	**(*n* = 25)**	**(*n* = 22)**	**(n = 9)**	**(*n* = 19)**
Amphetamine	1/1[a]	0/0	30/30[a]	0/3	2/3[a]	0/0	2/4[a]
NicAlert[g]	0/4	0/0	0/2	1/3	1/3	0/0	1/1

Notes: 11-nor-9-carboxy-tetrahydrocannabinol = THCCOOH, Δ9-tetrahydrocannabinol = THC, cannabidiol = CBD, cannabinol = CBN, Δ9-tetrahydrocannabivarin = THCV; ETG = ethyl glucuronide

[a]Positive results are consistent with the youth's prescription medication.

[b]Variation in analyte n due to insufficient quantity of hair (e.g., norcocaine; THCV).

[c]Other opioids tested for (fentanyl, codeine, morphine, 6-acetylmorphine, hydrocodone, hydromorphone, and oxycodone) were negative for all.

[d]Other cocaine metabolites tested for (cocaethylene, metahydroxycocaine, orthohydroxycocaine, and parahydroxycocaine) were all negative.

[e]Other amphetamines tested for (MDA, MDEA, and MDMA) were all negative.

[f]Seven drug classes (cocaine, opiates, cannabis, benzodiazepines, amphetamine, methamphetamine, and methadone) were tested as described in the primary manuscript. Only drug classes with a positive are displayed here.

[g]NicAlert is a urinary cotinine screen. Positive results on NicAlert here indicate urinary cotinine results at a level which indicates recent, personal nicotine exposure.