Table 1A: Summaries of cross-sectional, retrospective, and longitudinal studies assessing the potential cognitive, behavioral, psychopathological, and future substance use vulnerability outcomes of use of tobacco products by adolescents.

E = E-cigarette study; \* = estimation;(↑) = increase; (↓) = decrease; (NC) = no change; (+) = positive association; (-) = negative association; (≠) = no association; male = ♂; ♀= female; ⚧= transgender; Mage = mean age.

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| Authors | Study Type | N | Age | Gender % (♂/♀/⚧) | Findings |
| **Cognition** |
| Treur et al. (2015) | Cross-sectional; Longitudinal | Adults: 20,824Adolescents: 11,386 | Adult: 18-97 (Mage: 42; monozygotic twin Mage: 34)Adolescent: 8-18 (Mage: 15; monozygotic twin Mage: 15 (baseline), 17 (follow-up)) | Adult monozygotic twins: 26/74Adolescent monozygotic twins: 32/68 | Smoking ↑ attentional problems. Age of onset (-) attentional problems. |
| Tercyak et al. (2002) | Cross-sectional | 1,066 | 14-17\* | 48/52 | Inattention or hyperactivity/impulsivity (+) ever-smoking. Inattention ↑ current smoking likelihood. |
| Jacobsen et al. (2005) | Cross-sectional | 53 | 14-18 (Smoker Mage: 17.0; Non-smoker Mage: 16.6) | Smokers: 34/66Non-smokers: 38/62 | Acute abstinence ↑ withdrawal symptoms, depressed mood, anxiety, working memory, & verbal memory performance deficits. Smokers ↓ working memory & divided attention response performance. Age of smoking onset (+) cognitive performance. |
| McNeill et al. (1986) | Cross-sectional | 597 | 11-17 | 0/100 | Withdrawal effects (+) cotinine levels, depth of inhalation, & weekly cigarette consumption. Abstinence ↑ moodiness, restlessness, & hunger. |
| Rojas et al. (1998) | Cross-sectional | 249 | Mage: 16\* | 57/43 | Smoking level ♀<♂. Cravings (+) cotinine levels, depression (♂<♀), dependence (♀<♂) symptoms. Dependence, body weight change during adolescent cessation < adults. |
| DiFranza et al. (2007) | Longitudinal | Baseline: 1,246Follow-up: 970 | 11-14 (Mage: 12.2) | 48/52 | Relaxation after first inhale, depressed mood ↑ dependence, losing smoking autonomy. Extracurricular activities, ♀, & attention disorder symptoms ↓ dependence & losing autonomy. |
| Leventhal et al. (2015)E | Longitudinal | 2,530 | 13-15-Baseline: 13-14\* (E-cigarette ever-user Mage: 14.10; E-cigarette never-user Mage: 14.05)-Follow-up: 14-15\* | 47/53 | Cigarette use (+) parental education, peer smoking, impulsivity, other product use, delinquency, & smoking expectancies. Baseline e-cigarette use ↑ future combustible tobacco product use. Combustible tobacco product use ↑ follow-up e-cigarettes use. |
| Yin et al. (2016) | Cross-sectional | 36 | 15-18 (Smoker Mage: 16.9; Non-smoker Mage: 17.3) | 100/0 | Smokers ↑ No-Go trial response errors. Smokers ↓ inhibition control processing in No-Go trials. |
| Weiser et al. (2010) | Longitudinal | 20,221 | 18-21-Baseline: 18-Follow-up: 18-21 | 100/0 | Cognitive test scores in current smokers < former smokers < non-smokers. Daily cigarette consumption (-) cognitive scores. |
| **Psychopathology** |
| Zammit et al. (2003) | Longitudinal | 50,053 | 18-47\*-Baseline: 18-20-Follow-up: 18-47\* | 100/0 | Smoking by age 18 (≠) schizophrenia development within five years. Medium/heavy smokers ↓ schizophrenia risk five+ years post-conscription. Smoking (+) psychotic illness diagnoses. |
| Weiser et al. (2004) | Longitudinal | 14,248 | 18-34-Baseline: 18-Follow-up: 18-34 | 100/0 | Smoking & smoking heaviness (+) future hospitalization for schizophrenia. |
| McGrath et al. (2016) | Longitudinal; Retrospective | Baseline: 7,223Follow-up: 3,801 | 0-21 | 48/52 | Age of smoking onset (-) delusions, hallucinations, & psychotic disorder diagnoses. Hallucinations (-) age of smoking onset. Non-affective psychosis (≠) age of smoking onset. |
| Mustonen et al. (2018) | Longitudinal; Retrospective | 6,081 | 15-30-Baseline: 15-16-Follow-up: 15-30 | 48/52 | Adolescent smoking & psychosis (+) drug use, parental drug use, parental psychosis. Heavy smoking ↑ psychosis risk. Age of onset (-) future psychosis risk. |
| Jones et al. (2018) | Longitudinal | 5,300 | 12-20 | 44/56 | Smoking (≠) psychotic experiences at age 18. Early psychotic experiences (+) risk for later cigarette use. |
| Wu & Anthony (1999) | Longitudinal | 1,731 | 8-14-Baseline: 8-9-Follow-up: 13-14 | 50/50\* | Smoking (+) first occurrence of depressed mood risk. Depressed mood (≠) smoking onset. |
| Goodman & Capitman (2000) | Longitudinal | Non-smokers: 6,947Non-depressed: 8,704 | 11.43-21.23 (Non-smoker Mage: 15.32; Non-depressed Mage: 15.48) | Non-smokers: 51/49Non-depressed: 52/48 | Baseline non-depressed adolescent smokers ↑ follow-up high depressive symptoms. Moderate/heavy smoking black < white adolescents. |
| Albers & Biener (2002) | Longitudinal | 522 | 12-19-Baseline: 12-15 (Mage: 13.49)-Follow-up: 16-19 | 50/50 | Baseline smokers ↑ follow-up depressive symptoms. |
| Needham (2007) | Longitudinal | 10,828 | 12-28-Baseline: 12-18 (Mage: 15.28)-Follow-up: 13-28 | 47/53 | Smoking (+) depressive symptoms. Smoking progression (+) depressive symptom changes (♀ only). Baseline smoking frequency (+) depressive symptom decline rate. |
| Ilomäki et al. (2008) | Cross-sectional; Retrospective | 508 | 12-17 (♂ Mage: 15.4; ♀ Mage: 15.5) | 41/59 | Depressive disorder (+) daily smoking (♀<♂). Smoking (+) conduct & oppositional defiant disorders. Age of smoking onset in ♀ with substance use disorder < ♂ with substance use disorder < those without substance use disorder. |
| Audrain-McGovern et al. (2009) | Longitudinal | 1,093 | 14-18-Baseline: 14\*-Follow-up: 15-18\* | 47/53\* | Baseline depression & peer smoking ↑ follow-up smoking & smoking progression.Smoking ↑ deceleration of depression symptoms. |
| Morrell et al. (2010) | Cross-sectional | 1,214 | Mage: 18 | 40/60 | Depression & anhedonia ↑ smoking negative reinforcement expectancies. Depression or anhedonia ↑ smoking likelihood in (♀ only). |
| Slomp et al. (2019) | Cross-sectional | 988 | 11-17 (Mage: 13.5) | 56/44 | Smokers ↑ suicide ideation (♂<♀), anxiety & depression symptoms. |
| Brown et al. (1996) | Cross-sectional; Longitudinal; Retrospective | Baseline: 1,70913-month follow-up: 1,507 | 14-18 (Mage: 16.6 (baseline)) | 48/52 (baseline) | Age of onset (+) future drug abuse. Smoking ↑ MDD risk. |
| Stein et al. (1996) | Longitudinal | 461 | 12-27\*-Baseline: 12-15\*-Follow-up: 16-27\* | 29/71 | Middle adolescent & older smoking (+) depressed mood. Early adolescent smoking (+) sociability, cheerfulness, & extroversion. |
| Choi et al. (1997) | Longitudinal | 792 | 12-22-Baseline: 12-18-Follow-up: 15-22 | 37/63 | Baseline current smoking ↑ depressive symptoms risk. Baseline experimental smoking ↑ depression symptom risk (♀ only). |
| Windle & Windle (2001) | Longitudinal | 1,218 | 15-18\*-Baseline: 15-17\* (Mage: 15.54)-Follow-up: 16-18\* | 52/48 | Heavy baseline smoking (+) follow-up depressive symptoms. High depression symptomology (+) follow-up smoking. |
| Brook et al. (2002) | Longitudinal | 736 | 14-27-Baseline: 14 (Mage: 14.05)-Follow-up: 16-27 | 50/50 | Early/late adolescent smoking ↑ adulthood MDD risk. Early adulthood smoking (NC) MDD risk. |
| Brook et al. (2004) | Longitudinal | 688 | 14-27-Baseline: 14-Follow-up: 17-27 | 49/51 | Adolescence/young adulthood smoking ↓ follow-up depressive symptom number. |
| Galambos et al. (2004) | Longitudinal | 1,322 | 12-19-Baseline: 12-19-Follow-up: 16-23 | 49/51 | Earlier smoking ↑ future depression symptom risk. Earlier depression symptoms emergence ↑ future high frequency smoking. Smoking level (+) depressive symptom development. |
| Duncan & Rees (2005) | Longitudinal | 13,068 | 13-22-Baseline: 11-21 (♂ Mage: 15.62; ♀ Mage: 15.46)-Follow-up: 12-22 (♂ Mage: 16.53; ♀ Mage: 16.37) | 52/48 | Baseline smoking (+) baseline depression, follow-up depression symptoms. |
| Rodriguez et al. (2005) | Longitudinal | 925 | 14-18-Baseline: 14-Follow-up: 15-18 | 46/54 | Baseline high depression, smoking (+) decelerated depression symptom development. Baseline moderate depression, smoking (+) accelerated depression symptom development. |
| Boden et al. (2010) | Longitudinal | 1,265 | 17-25-Baseline: 17-18-Follow-up: 20-25 | 50/50 | Nicotine dependence (+) depressive symptoms. Depressive symptoms (≠) nicotine dependence. |
| Moon et al. (2010) | Longitudinal | 5,625 | 12-19(Mage: 16.04)-Baseline: 12-18-Follow-up: 13-19 | 49/51 | Baseline depressive symptoms (+) future smoking. Smoking (+) follow-up depressive symptoms. |
| Jamal et al. (2011) | Cross-sectional; Retrospective | 1,055 | 18-65 (Early onset smoker Mage: 42.0; Late onset smoker Mage: 47.1) | 33/67 | Late-onset smokers risk of early depression/anxiety diagnosis < early-onset smokers. Risk of early depression/anxiety diagnosis ♂ smokers < ♀ smokers. |
| Beal et al. (2014) | Longitudinal | 262 | 11-20-Baseline: 11-17-Follow-up: 15-20 | 0/100 | Baseline smoking ↑ future depression symptom risk. Depression symptoms (≠) future smoking. |
| Gage et al. (2015) | Longitudinal | 1,791 | 16-18-Baseline: 16-Follow-up: 18 | 42/58 | Smoking (≠) future depression, anxiety. |
| Wang et al. (1996) | Longitudinal | 3,811 | 12-21-Baseline: 12-18-Follow-up: 15-21 (Mage: 16.5) | N/A | Smoking (+) depression. Depression (+) smoking. |
| Repetto et al. (2005) | Longitudinal | 623 | 14-23-Baseline: 14-17 (Mage: 14.55)-Follow-up: 15-23 | 49/51 | Smoking trajectory (≠) future depressive symptoms. Depression symptoms change (+) smoking trajectory. |
| Clark et al. (2007) | Longitudinal | 1,513 | 11-16-Baseline: 11-14-Follow-up: 13-16 | 47/53 | Baseline smoking (≠) follow-up depressive symptom risk. |
| Munafò et al. (2008) | Longitudinal | 13,405 | 13-19-Baseline: 13-18 (Mage: 15)-Follow-up: 14-19 | 49/51 | Baseline depression (+) follow-up smoking (not in baseline regular smokers). Baseline smoking (≠) follow-up depression. |
| Hu et al. (2011) | Longitudinal | 660 | 11-17-Baseline: 11-17 (Mage: 14.7)-Follow-up: 13-19 | 46/54 | Baseline dependence, positive smoking experiences, perceptions of peer smoking, conduct problems (+) follow-up dependence. Baseline depression (≠) future nicotine dependence. Baseline depression (≠) future depression. |
| Strong et al. (2014) | Longitudinal | 703 | 15-43-Baseline: 15-16-Follow-up: 32-43 | 49/51 | Baseline smoking (≠) adulthood MDD. |
| **Future Substance Use** |
| Stanton (1995) | Longitudinal | 1,139 | 15-18-Baseline: 15-Follow-up: 18 | 51/49\* | Smoking at age 15 (+) smoking at age 18. Daily smoking at age 15, smoking to relieve withdrawal, & appetite & weight changes ♂<♀. |
| Everett et al. (1999) | Cross-sectional; Retrospective | 13,858 | 16-18\* | N/A | Smoking onset (<15-years-old) ♀ < ♂. Ever-smoking & younger age of onset in black < white & Hispanic adolescents. Age of onset (-) smoking frequency. |
| Colder et al. (2001) | Longitudinal; Retrospective | 323 | 11-16-Baseline: 11-12 (Mage: 12)-Follow-up: 12-16 | 48/52 | Five adolescent smoking trajectories: 1) stable light smoking, 2) stable smoking, 3) early rapid escalation, 4) late moderate escalation, & 5) late slow escalation. Early onset smoking ↑ future smoking. |
| Riggs et al. (2007) | Longitudinal | 1,017 | 12-28-Baseline: 12-Follow-up: 12-28 | 45/55 | Early onset heavy smoking ↑ future smoking dependence. Smoking frequencies diverged at age 15 (occasional vs. late heavy smokers) & 12 (early heavy smokers). |
| Dierker et al. (2012) | Cross-sectional; Retrospective | 10,123 | 13-17 (Mage: 15.2) | N/A | Age of onset (+) weekly, daily use. Faster smoking escalation (+) dependence. Age of onset, dependence ♂ < ♀. |
| Buchmann et al. (2013) | Longitudinal | 213 | 15-22-Baseline: 15-Follow-up: 22 | 47/53 | Age of first use (-) positive smoking experiences. Age of first cigarette, age of pleasurable smoking experiences (-) smoking in young adulthood smoking, smoking frequency, & level of dependence. |
| Taioli & Wynder (1991) | Retrospective | 42,002 | N/A | 72/28 | Age of onset (-) number of cigarettes smoked/day in adulthood. |
| Klein et al., (2013) | Retrospective | 485 | 18-70 (Mage: 36.4) | 57/43 | Age of onset, purchase of first cigarette, latency between first & second cigarette (-) number of cigarettes smoked per week in adulthood. Age of onset (-) future smoking during illness, smoking to function, perceived benefits of smoking. |
| Lanza & Vasilenko (2015) | Retrospective | 15,748 | 18+ (Mage: 46.4) | 43/57 | Age of onset ♂ < ♀. Age of onset (-) adult dependence. Rates of adolescent onset-associated adult dependence ♂ < ♀. |
| DiFranza et al. (2000) | Longitudinal | Baseline: 681Follow-up: 626 | 12-15 (Mage: 12.6) | 52/48 | Dependence symptoms reported in 62% of adolescents before daily smoking. Dependence symptoms reported in 25% of monthly smokers within two weeks of onset; 22% before end of first smoking month. |
| DiFranza et al. (2002) | Longitudinal | Baseline: 679Follow-up: 471 | 12-15 (Mage: 13.1) | 51/49 | Smoking dependence symptoms were reported after first (18%), monthly (33%), weekly (49%), & pre-daily (70%) use. Symptom count, onset ♂ < ♀. Baseline dependence symptoms ↑ follow-up current smoking. |
| Caris et al. (2009) | Cross-sectional | 30,490 | 12-18 | 48/52 | Tobacco use ↑ cannabis use opportunities, cannabis experimentation |
| Lewinsohn et al. (1999) | Longitudinal | 684 | 17-24-Baseline: 17-18\*-Follow-up: 18-24\* | 40/60 | Smoking ↑ future alcohol, cannabis, & other drug disorder risk. Longer duration of smoking cessation following daily smoking ↓ AUD risk. Early smoking onset ↑ future substance use disorder risk. |
| Barrington-Trimis et al. (2016)E | Longitudinal | 298 | 16-19-Baseline: 16.8-17.9\* (Median age: 17.4)-Follow-up: 18.3-19.0 (Median age: 18.6) | 58/42 | Baseline e-cigarette use ↑ follow-up combustible tobacco product use. |
| Azagba et al. (2017)E | Cross-sectional | 25,637 | 12-19 | 50/50 | E-cigarette experimentation ↓ cigarette smoking susceptibility |
| Miech et al. (2017)E | Longitudinal | 347 | 17-19\* (Modal age: 19 (follow-up)) | 44/56 | E-cigarette users ↓ perceived cigarette risk, ↑ follow-up cigarette use. |
| Spindle et al. (2017)E | Longitudinal | 3,757 | 18+ (Baseline Mage: 18.5) | 44/66 | Baseline e-cigarette use, stress, & impulsivity (+) future cigarette use onset. E-cigarette use (+) ♂, cannabis use. Dual use (+) ♂, other tobacco product use, impulsivity. |
| Wills et al. (2017)E | Longitudinal | 2,338 | 14-17-Baseline: 14-15 (Mage: 14.7)-Follow-up: 15-17 (Mage: 15.8) | 47/53 | Baseline e-cigarette use (+) follow-up cigarette use risk. Level of e-cigarette use (+) follow-up regular cigarette use. Baseline e-cigarette use (≠) follow-up cigarette use reduction. |
| Barrington-Trimis et al. (2018)E | Longitudinal | 6,258 | 14-18\* | 46/54 | Baseline e-cigarette use ↑ combustible smoking onset, frequency of combustible use. Baseline e-cigarette use (NC) follow-up combustible smoking reduction. |
| Berry et al. (2019)E | Longitudinal | 6,123 | 12-18-Baseline: 12-15 (Mage: 13.4)-Follow-up: 15-18 | 51/49 | Baseline e-cigarette, non-cigarette tobacco product use ↑ follow-up combustible cigarette onset, current use risk. Baseline combustible cigarette use ↑ follow-up e-cigarette use risk. |
| Vogel et al. (2019)E | Longitudinal | Baseline: 1736-month follow-up: 12012-month follow-up: 127 | 13-19Baseline: 13-18 (Mage: 16.6)Follow-up: 14-19 | 75/25 | Baseline e-cigarette use (+) follow-up nicotine use, dependence, exposure, & the use of combustible cigarettes & high-yield nicotine devices. |
| Vogel et al. (2020)E | Cross-sectional; Longitudinal | 444 | 17-18\* (Mage: 17.48) | 51/49 | E-cigarette dependence < combustible cigarette dependence in dual users. E-cigarette dependence in e-cigarette only users < dual users. Baseline e-cigarette dependence (+) follow-up combustible & e-cigarette use. |
| Cassidy et al. (2018)E | Longitudinal | 1,313 | Baseline Mage: 18.6 | 45/55 | E-cigarettes ever-use ↑ follow-up cannabis vaping onset. Baseline cannabis & cigarette ever-use ↑ follow-up e-cigarette use. |
| Dai et al. (2018)E | Longitudinal | 10,364 | 12-18-Baseline: 12-17-Follow-up: 13-18 | 51/49 | E-cigarette use ↑ follow-up cannabis use likelihood. Young adolescent e-cigarette use (+) future cannabis use. |
| Jackson et al. (2020)E | Cross-sectional | 49 | 16-20 (Mage: 18.7) | 61/37/2 | Menthol e-cigarette flavor preference < green-apple flavor. Preference for high nicotine concentration e-cigarette < low nicotine concentration. |
| Boykan et al. (2019)E | Cross-sectional | 265 | 12-21 (primarily 15-17) | 34/64/2 | Urinary cotinine levels in weekly < daily smokers. Daily e-cigarette users ↑ pod-based e-cigarette device use. Pod-based e-cigarette users ↑ higher urinary cotinine levels. |
| Goldenson et al. (2017)E | Longitudinal | 181 | 15-17\* (Mage: 16.1) | 53/47 | Baseline nicotine concentration used (+) follow-up smoking & e-cigarette use, frequency of use, intensity of use. |
| Goniewicz et al. (2019)E | Cross-sectional | 22 | 12-21 (Mage: 16.8) | N/A | Nicotine delivered per puff of older generation e-cigarettes < newer generation e-cigarettes. Urine cotinine levels combustible cigarette users < e-cigarette users (see (Benowitz et al., 2018)). |

Table 1B: Summaries of cross-sectional, retrospective, and longitudinal studies assessing the potential structural, and functional vulnerability outcomes of use of tobacco products by adolescents. E = E-cigarette study; \* = estimation; (↑) = increase; (↓) = decrease; (NC) = no change; (+) = positive association; (-) = negative association; (≠) = no association; male = ♂; female = ♀; Mage = mean age.

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| Authors | Study Type | N | Age | Gender % (♂/♀) | Findings |
| **Structural** |
| Akkermans et al. (2017) | Longitudinal | 89 | 9.5-27.6-Baseline: 9.5-24.2 (Smoker Mage: 17.9 for smokers; Non-smoker Mage: 17.6)-Follow-up: 12.9-27.6 (Smoker Mage: 21.3; Non-smoker Mage: 20.9) | -Smokers: 63/36-Non-smokers: 55/45 | Early onset smoking ↓ frontal cortical thickness. Smoking ↑ inattention. |
| Jacobsen et al. (2007b) | Cross-sectional | 67 | 13-18 (Mage: 16.5\*) | 39/61 | Smoke exposure (+) cortex, corpus callosum, longitudinal fasciculus, internal capsule FA. Auditory attention reaction time (+) internal capsule & temporal lobe FA. |
| Li et al. (2017) | Cross-sectional | 61 | 16-21 (Smoker Mage: 19.4; Non-smoker Mage: 19.5) | 100/0 | Smoking ↑ incongruent Stroop task errors. Errors (+) ACC-insula tract FA. Insula-ACC RSFC (-) smoking duration. |
| Li et al. (2015) | Cross-sectional | 49 | 14-23 (Smoker Mage: 19.7; Non-smoker Mage: 19.3) | 100/0 | Smoking ↓ frontal cortex cortical thickness. Smoking dependence (-) DLPFC thickness. Lifetime exposure (-) OFC thickness. |
| Chaarani et al. (2019) | Cross-sectional; Longitudinal | GMV analysis: 838FA analysis: 676Genetic analysis: 1,417 | -Baseline Mage:14.5-Follow-up Mage:16 | GMV and FA analysis:-Smokers: 50/50 smokers-Non-smokers: 52/48Genetic analysis:-Smokers: 48/52-Non-smokers: 50/50 | Smoking (-) ventromedial PFC GMV. GMV (≠) future smoking. *CHRNA* polymorphisms ↓ GMV. Smoking (-) corpus callosum FA. |
| van Ewijk et al. (2015) | Cross-sectional | 186 | 14-24 (Regular smoker Mage: 18.8; Irregular smoker Mage: 19.1; Non-smoker Mage: 16.7) | Regular smokers: 78/22Irregular smokers: 56/44Non-smokers: 62/38 | Regular smokers ↑ FA, ↓ mean diffusivity in the basal ganglia. Effects of smoking & ADHD on FA showed regional overlap but different directionality. |
| Yu et al. (2016) | Cross-sectional | 45 | 14-23 (Smoker Mage: 19.6; Non-smoker Mage: 19.3) | 100/0 | Smokers ↑ FA & axial diffusivity, ↓ radial diffusivity. Corona radiata FA (+) dependence & smoking duration. Corona radiata radial diffusivity (-) smoking duration. |
| **Functional** |
| Jacobsen et al. (2007c) | Cross-sectional | 181 | 13-18 (Mage: 16.6\*) | 38/62 | Smokers ↑ depression symptoms, drug use rates, auditory attention brain region activation during task performance. Smokers ↓ intelligence. Smoke exposure (-) auditory lexical discrimination performance. |
| Bi et al. (2017) | Cross-sectional | Functional connect-ivity: 80Cognitive perform-ance: 56 | 15-24 (Smoker Mage: 19.62; Non-smoker Mage: 19.58) | 100/0 | Smokers ↑ incongruent Stroop task errors, ↓ RSFC between anterior insula with PFC, amygdala, & striatum.Insula connectivity (-) cravings, dependence, Stroop errors committed, & smoking duration. |
| Li et al. (2017) | Cross-sectional | 61 | 16-21 (Smoker Mage: 19.4; Non-smoker Mage: 19.5) | 100/0 | Smoking ↑ incongruent Stroop task errors. Errors (+) ACC-insula tract FA. Insula-ACC RSFC (-) smoking duration. |
| Galván et al. (2011) | Cross-sectional | 50 | 15-21 (Smoker Mage: 19.32; Non-smoker Mage: 19.00) | 58/42 | Smoking (NC) Stop-Signal task performance. Nicotine dependence (-) response inhibition neural activation. Stop-signal reaction times (-) cortical activity. |
| Lee et al. (2005) | Cross-sectional | 8 | 16-18 (Mage: 17.13) | 100/0 | 2D smoking cues ↑ PFC, ACC, supplementary motor area, temporal cortex, & occipital lobe activity. 3D virtual reality smoking cues ↑ frontal, occipital, & temporal gyri activation. |
| Rubinstein et al. (2011b) | Cross-sectional | 24 | 13-17 (Mage: 16.3) | 58/42 | Smokers ↑ smoking cue-induced activation in mesolimbic reward regions, the parahippocampal & occipital gyri, & medial occipital regions. |
| Rubinstein et al. (2011a) | Cross-sectional | 24 | 13-17 (Mage: 16.3) | 58/42 | Smokers ↓ food cue-induced activation in the insula, putamen, inferior frontal cortex & Rolandic operculum. |
| Dinn et al. (2004) | Cross-sectional | 139 | 17-25 (Mage: 18.6) | 29/71 | Current smokers (NC) major psychopathology & ADHD symptomology. Smokers ↑ orbitofrontal dysfunction, other drug abuse risk. |
| Jacobsen et al. (2007a) | Cross-sectional | 93 | Smoker Mage: 16.9Non-smoker Mage: 16.6 | 38/62 | Smoking ↓ high-load verbal working memory accuracy. Smoking ↑ activation of memory regions. Abstinence ↓ memory network efficiency. |
| Chen et al. (2018)E | Cross-sectional | 29 | 14-21 (Mage: 16.96) | 57/43 | E-cigarette advertisements ↑ smoking desire, & activation of cognitive control, reward, visual processing & attention, & memory brain regions. |
| Mashhoon et al. (2018) | Cross-sectional; Retrospective | 30 | 22-40 | 50/50 | Late onset smoker cortical smoking cue reactivity during withdrawal < early onset smoker. Late onset smokers baseline cigarette craving < early onset smokers. |

Table 2A: Summaries of cross-sectional, retrospective, and longitudinal studies assessing the potential cognitive, behavioral, psychopathological, and future substance use vulnerability outcomes of use of alcohol use by adolescents. \* = estimation; (↑) = increase; (↓) = decrease; (+) = positive association; (-) = negative association; (≠) = no association; male = ♂; ♀= female; Mage = mean age.

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| Author | Study Type | N | Age | Gender % (♂/♀) | Findings |
| Cognition |
| Field et al. (2007) | Cross-sectional | 90 | 16-18 (Mage: 16.8) | 92/8 | Heavy drinking (+) inhibitory control deficits & attentional bias for alcohol cues. |
| Melaugh McAteer et al. (2015) | Cross-sectional | 44 | 16-19 (Mage: 17.1) | 66/34 | Social drinkers (+) attentional bias for alcohol cues. |
| Squeglia et al. (2009) | Longitudinal | 76 | 12-17-Baseline: 12-14-Follow-up: 15-17 | 62/38 | More drinking days in the past year ↓ visuospatial function (♀); more hangover symptoms ↓ sustained attention (♂) |
| Ruan et al. (2019) | Longitudinal | 212 | 14-19-Baseline: 14-Follow-up: 19 | 57 /43 | Binge-drinking ↑ impulsivity at age 19 & ↓ developmental trajectory of impulsivity. |
| Jones et al. (2017) | Longitudinal | 116 | 10-25-Baseline: 10-17 (Mage: 14.2)-Follow-up: 18-25 | 53/47 | More life-time drinks in binge-drinkers ↑ impulsive choice. |
| Brown et al. (2000) | Cross-sectional | 57 | 15-16 (AUD Mage: 16.2; Non-AUD Mage: 15.9) | 58/42 | Lifetime alcohol withdrawal (+) verbal & non-verbal retrieval impairments; recent withdrawal (+) visuospatial functioning impairments. |
| Hanson et al. (2011) | Longitudinal | 213 | 13-27-Baseline: 13-18 (Mage: 5.7)-Follow-up: 16-27 | 54/46 | Heavy alcohol use (+) verbal learning & memory deficits. |
| Parada et al. (2012) | Cross-sectional | 122 | 18-20 (Binge drinking ♂ Mage: 19.0; Binge drinking ♀ Mage: 18.7; Non-binge drinking ♂ Mage: 18.6; Non-binge drinking ♀ Mage: 18.8) | 52/48 | Binge drinkers ↓ verbal working memory performance & ↑ perseveration. |
| Carbia et al. (2017a) | Longitudinal | 155 | 18-25-Baseline: 18-19 (Mage: 18.7)-Follow-up: 24-25 | 49/51 | Stable binge drinking (+) persistent impairments in immediate & delayed recall. Impairments may improve with long-term abstinence; long-term ex-binge drinker did not display difficulties compared to short-term ex-binge drinkers. |
| Carbia et al. (2017b) | Longitudinal | 155 | 18-25-Baseline: 18-19 (Mage: 18.7)-Follow-up: 24-25 | 49/51 | Stable binge drinking (+) perseverative errors & ↓ working memory span. ↓ working memory improved with or without alcohol abstinence. |
| Khurana et al. (2013) | Longitudinal | 358 | Range N/A-Baseline Mage: 11.4-Follow-up: 4 years later | 48/52 | Greater impulsivity underlying weaker working memory (+) alcohol use over four years. |
| Nguyen-Louie et al. (2016) | Longitudinal | 112 | 12-22-Baseline: 12-16 (Extreme binge drinker Mage: 13.8; Binge drinker Mage: 19.6; Moderate drinker Mage: 19.5)-Follow-up: 18-22 (Extreme binge drinker Mage: 19.7; Binge drinker Mage: 19.3; Moderate drinker Mage: 19.7) | 64/36 | Extreme binge drinking deficits (+) in verbal learning & short delayed recall compared to moderate drinkers. |
| Nguyen-Louie et al. (2017) | Longitudinal | 215 | 12-22-Baseline: 12-15 (Mage: 13.6)-Follow-up: 19-22\* (Mage: 20.2) | 59/41 | Early onset of first drinking (+) psychomotor speed & visual attention impairments, while earlier onset of weekly drinking (+) impairments in cognitive inhibition & working memory. |
| Mahedy et al. (2018) | Longitudinal | 4,466 | 15-17-Baseline Mage: 15.5-Follow-up Mage: 17.8 | N/A | Adolescent frequent/binge drinking (+) working memory impairments at a three-year follow-up. |
| Psychopathology |  |  |  |  |  |
| Briere et al. (2011) | Longitudinal | 6,589 | 12-16-Baseline: 12-13(Mage: 12.8)-Follow-up: 15-16 | 48/52 | Simultaneous use of alcohol & cannabis in grade 10 (+) substance-related issues the following year compared to concurrent use. |
| Edwards et al. (2014) | Longitudinal | 7,100 | 13-18-Baseline: 13-15-Follow-up Mage: 17.8 | 49/51 | Alcohol use (+) later depression, but not anxiety after adjustment for confounders. |
| Mason et al. (2008) | Longitudinal | 429 | 11-22-Baseline: 11 (Mage: 11.0)-Follow-up: 22 (Mage: 21.6) | 48/52 | Problem use, but not alcohol intake (+) young adult MDD. |
| Fasteau et al. (2017) | Longitudinal | 1,910 | 16-23-Baseline: 16-Follow-up: 23 | 33/67 | Self-reported alcohol use (+) future onset of hypomanic/manic symptoms. |
| Blumenthal et al. (2010) | Cross-sectional | 50 | 12-17 (Mage: 16.4) | 48/52 | Heightened social anxiety (+) coping-related drinking motives. |
| Schleider et al. (2019) | Longitudinal | 2,100 | 13-17-Baseline: 13-Follow-up: 13-17 | 100/0 | Higher depression severity modestly ↑ alcohol use from ages 13 to 17. Alcohol use modestly ↓ odds of depression at ages 14 & 16. Anxiety severity (≠) alcohol use |
| Parrish et al. (2016) | Longitudinal | 674 | 14-16-Baseline: 14-Follow-up: 16 | 50/50 | Alcohol use at age 14 (+) overall internalizing symptoms. Overall internalizing symptoms at age 14 (+) alcohol use. |
| Kaplow et al. (2001) | Longitudinal | 936 | 9-17-Baseline: 9-13-Follow-up: 13-17 | 55/45 | Early generalized anxiety symptomology (+) risk for the initiation of alcohol use. Early depressive symptomology (+) risk for the initiation of alcohol use in adolescence. |
| Future Substance Use |
| Viner and Taylor (2007) | Longitudinal | 4,911 | 16-30-Baseline: 16-Follow-up: 30 | 41/59 | Binge drinking (+) risk of alcohol dependence, illicit drug use, & social adversity at age 30. |
| Pampati et al. (2018) | Longitudinal | 2,359 | 13-32-Baseline: 13-21-Follow-up: 14-32 | 46/54 | Higher cannabis & alcohol use frequency (+) persistence of cannabis use. |
| Enstad et al. (2019) | Longitudinal | Study 1: 329Study 2: 789 | Study 1:14-19-Baseline: 14-15 (Mage: 14.6)-Follow-up: 18-19 (Mage: 18.9)Study 2:13-24-Baseline: 13.8-16.2 (Mage: 14.9)-Follow-up: 21.6-24.6 (Mage: 22.9) | Study 1:40/60Study 2:N/A | Early onset drinking & early onset of excessive drinking (+) risk of alcohol-related problems in late adolescence/young adulthood. |

Table 2B: Summaries of cross-sectional, retrospective, and longitudinal imaging studies assessing the potential structural and functional vulnerability outcomes of use of alcohol by adolescents.\* = estimation; (↑) = increase; (↓) = decrease; (NC) = no change; (+) = positive association; (≠) = no association; male = ♂; female = ♀; Mage = mean age.

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| --- | --- | --- | --- | --- | --- |
| Author | Study Type | N | Age | Gender % (♂/♀) | Findings |
| Functional |
| Ahmadi et al. (2013) | Cross-sectional | 92 | 18-20 (Heavy drinker Mage: 19.0; Light drinker Mage: 18.8) | 47/53 | Heavy drinkers ↓ activation during Go/No-Go Task & ↑ impulsivity. |
| Aloi et al. (2019) | Cross-sectional | 150 | 14-18 (Mage: 16.1) | 61/39 | CUD & AUD ↓ activity in brain regions implicated in error detection & reward processing. |
| Norman et al. (2011) | Longitudinal | 38 | 12-20\*-Baseline: 12-14 (Transitioned to use Mage: 13.9; Control Mage: 13.4)-Follow-up: 16-20\* (Transitioned to use Mage: 18.0; Control Mage: 17.7) | 50/50 | Lower activation during Go/No-Go task at baseline (+) transition into heavy alcohol consumption. |
| Wetherill et al. (2013) | Longitudinal | 40 | 11-20-Baseline: 11-16 (Heavy drinker Mage: 14.7; Non-heavy drinker Mage: 14.1)-Follow-up: 14-20 (Heavy drinker Mage: 18.5; Non-heavy drinker Mage: 17.6) | 55/45 | Transition into heavy drinking (+) ↓ activation of inhibitory circuitry at baseline & ↑ activation after onset of heavy drinking. |
| Schweinsburg et al. (2010) | Cross-sectional | 24 | 16-18 (Binge drinker Mage: 18.2; Non-binge drinker Mage: 17.8) | 75/25 | Binge drinking (+) deficits in recall memory & ↑ activation of frontal & parietal regions, & lack of activation of left hippocampus during novel encoding. |
| Tapert et al. (2004) | Cross-sectional | 34 | 15-17 (AUD Mage: 16.8; Non-AUD Mage: 16.5) | 62/38 | AUD (+) differences in brain response to spatial working memory task despite adequate task performance. |
| Squeglia et al. (2012a) | Longitudinal | 40 | 12-21-Baseline: 12-19 (Heavy drinking transitioner Mage: 15.1; Continuous non-drinker Mage: 17.8)-Follow-up: 12-21 | 70/30 | Lower activation in the frontal & parietal response to working memory (+) transition into heavy drinking. Heavy drinking (+) frontal & parietal response over time. |
| Caldwell et al. (2005) | Cross-sectional | 37 | 14-17 (♂ AUD Mage: 16.6; ♀ AUD Mage: 16.9; ♂ non-AUD Mage: 16.6; ♀ non-AUD Mage: 16.2) | 62/38 | Differences in brain activation in temporal regions were seen in ♂ & ♀ participants compared to each other & controls during a spatial working memory task despite (NC) in task performance |
| Squeglia et al. (2011) | Cross-sectional | 95 | 16-19 (♂ binge drinker Mage: 18.1; ♀ binge drinker Mage: 17.8; ♂ non-binge drinker Mage: 17.7; ♀ non-binge drinker Mage: 18.1) | 61/39 | Binge drinking (-) activation in frontal, temporal & cerebellar regions during a spatial memory task, (+) deficits in sustained attention & working memory (♀ only). |
| Aloi et al. (2018) | Cross-sectional | 97 | 14-18 (Mage: 16.1) | 62/38 | AUD, but not CUD, symptom severity (+) amygdala activity to emotional stimuli. |
| Jurk et al. (2018) | Longitudinal | 131 | 14-18-Baseline: 14-Follow-up: 16-18 | 50/50 | Neural & behavioral measures of cognitive control at baseline **(≠)** alcohol use at age 18. |
| Peters et al. (2017) | Longitudinal | Baseline: 292Follow-up: 254 | 8-27-Baseline: 8-25 (Mage: 14.1)-Follow-up: 10-27 | 48/52 | Greater connectivity between the amygdala & OFC at baseline (+) alcohol use after a two-year follow-up. |
| Jones et al. (2016) | Longitudinal | 26 | 13-19\*-Baseline: 13-16 (Mage: 14.9)-Follow-up: 16-19\* (Mage: 17.4) | 62/38 | Binge-drinking (-) activation in the dorsal striatum during decision-making. Lower fronto-parietal activation (+) subsequent emergence into alcohol drinking. |
| Morales et al. (2018) | Longitudinal | 47 | 14-18\*-Baseline: 14-15 (Mage: 15.1)-Follow-up: 14-18\* | 40/60 | Greater activation in the nucleus accumbens, precuneus, & occipital cortex during risky decision-making (+) earlier initiation of binge drinking. |
| Cservenka et al. (2015) | Longitudinal | 34 | 12-18-Baseline: 12-16 (Mage: 14.9)-Follow-up: 14-18\* (Mage: 16.8) | 58/42 | Binge drinking (-) activity in the left cerebellum. (NC) in ventral striatum activity was observed. |
| Swartz et al. (2020) | Longitudinal | 262 | 16-18-Baseline: 16 (♂ Mage: 16.9; ♀ Mage: 18.9)-Follow-up: 18 | 51/49 | Differential activation patterns in reward-related neural regions (+) alcohol use from age 16 to 18. |
| Tapert et al. (2003) | Cross-sectional | 30 | 14-17 (AUD Mage: 17.0; Non-AUD Mage: 16.4) | 60/40 | AUD (+) brain activation in the left anterior, limbic, & visual systems to alcohol cues. Activation (+) drinks per month & desire to drink. |
| Dager et al. (2014) | Longitudinal | 43 | 18-22-Baseline: 18-21 (Heavy drinker Mage: 18.7; Transitioner Mage: 18.2; Moderate drinker Mage: 18.5)-Follow-up: 19-22 | 46/54 | Escalation of alcohol drinking from moderate to heavy (+) BOLD response to alcohol cues in brain regions implicated in cue-reactivity. |
| Brumback et al. (2015) | Longitudinal | 38 | 16-19-Baseline: 16-19 (Heavy drinker Mage: 17.9; Non-heavy drinker Mage: 17.4)-Follow-up: 16-19 | 46/54 | Heavy drinking (+) BOLD activation to alcohol cues in brain regions implicated in reward processing & decision-making, which disappeared after a month of abstinence |
| Structural |  |  |  |  |  |
| Squeglia et al. (2014) | Longitudinal | 40 | 12-21-Baseline: 12-17 (Heavy drinker Mage: 15.1; Non-heavy drinker Mage: 15.0)-Follow-up: 15-21 (Heavy drinker Mage: 18.0; Non-heavy drinker Mage: 17.2) | 63/37 | Transition to heavy-drinking ↓ frontal brain region volumes at baseline & ↑ volume reductions in subcortical & temporal regions. |
| Cheetham et al. (2014) | Longitudinal | 98 | 11-17-Baseline: 11.8-13.6 (Mage: 12.7)-Follow-up: 15.4-17.6 (Mage: 16.5) | 48/52 | Smaller left dorsal & rostral paralimbic ACC at age 12 (+) alcohol-related problems at age 16. |
| Jacobus et al. (2009) | Cross-sectional | 42 | Age: 16-19 (Mage: 17.9) | 86/14 | Binge drinkers ↓ white matter integrity in eight regions. |
| McQueeny et al. (2009) | Cross-sectional | 28 | 16-19 (Binge drinker Mage: 18.1; Non-binge drinker Mage: 18.0) | 86/14 | Binge drinking (-) FA in the corpus callosum, cerebellar, temporal, & parietal white matter tracts. |
| Luciana et al. (2013) | Longitudinal | 55 | 14-22-Baseline: 14-19 (Alcohol initiator Mage: 16.7; Alcohol non-user Mage: 17.1)-Follow-up: 16-22 (Alcohol initiator Mage: 19.2; Alcohol non-user Mage: 18.6) | 55/45 | Alcohol initiation (+) greater **↓** in cortical thickness & blunted white matter development. |
| Cardenas et al. (2013) | Cross-sectional | 100 | -AUD Mage: 15.0-Non-AUD Mage: 14.8 | 44/56 | Adolescents with AUD ↑ FA in white matter tracts of the limbic system. |
| De Bellis et al. (2000) | Cross-sectional | 36 | 13.5-21 (Adolescent AUD Mage: 17.2; No adolescent AUD Mage: 17.0) | 42/58 | Adolescent onset AUD (+) with smaller left & right hippocampal volume. |
| De Bellis et al. (2005) | Cross-sectional | 42 | 13-21 (AUD Mage: 17.0; No AUD Mage: 16.9) | 57/43 | AUD (+) smaller PFC volume & PFC white matter volume; AUD (+) smaller cerebellar volumes in ♂. |
| Nagel et al. (2005) | Cross-sectional | 31 | 15-17 (AUD Mage: 16.8; Non-AUD Mage: 16.5) | 61/39 | AUD (+) smaller left hippocampal volume. Hippocampal volume ≠ alcohol consumption rates, suggesting premorbid volumetric differences. |
| Squeglia et al. (2012b) | Cross-sectional | 59 | 16-19 (♂ Binge drinker Mage: 18.6; ♀ Binge drinker Mage: 17.8; ♂ Non-binge drinker Mage: 17.9; ♀ Non-binge drinker Mage: 18.0) | 51/49 | Binge drinking (+) thicker left frontal cortices, which (+) visuospatial, inhibition, & attention deficits. |
| Lisdahl et al. (2013) | Cross-sectional | 106 | 16-19 (Binge drinker Mage: 18.0; Non-binge drinker Mage: 17.7) | 62/38 | Higher peak drinks in binge-drinkers (+) smaller gray & white cerebellar volumes. |
| Pfefferbaum et al. (2018) | Longitudinal | 483 | 12-23-Baseline: 12-21 (Heavy drinker Mage: 17.1; Moderate drinker Mage: 16.7; Maintained Low/No drinker Mage: 15.1; No/Low drinker Mage: 15.6)-Follow-up: 13-23 | 50/50 | Heavy drinking (+) accelerated frontal cortical gray matter trajectory. |

Table 3A: Summaries of cross-sectional, retrospective, and longitudinal studies assessing the potential cognitive, behavioral, psychopathological, and future substance use vulnerability outcomes of use of cannabis use by adolescents\* = estimation (↑) = increase; (↓) = decrease; (=) = same as control; (NC) = no change; (+) = positive association; (-) = negative association; (≠) = no association; male = ♂; female = ♀; Mage = mean age.

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| --- | --- | --- | --- | --- | --- |
| Author. | Study Type | N | Age | Gender % (♂/♀) | Findings |
| Cognition |
| Harvey et al. (2007) | Cross-sectional | 70 | 13-18 (Mage: 16.2) | 40/60 | Regular cannabis use (+) attention, spatial working memory & learning impairments. |
| Lane et al. (2007) | Cross-sectional | 52 | 14-18 (Cannabis user Mage: 16.8; Cannabis non-user Mage: 16.2) | 65/35 | Heavy cannabis smoking (+) problem-solving & response adaptation impairments. |
| Medina et al. (2007a) | Cross-sectional | 65 | 16-18 (Cannabis user Mage: 18.1; Cannabis non-user Mage: 17.9) | 74/26 | Cannabis use (+) poorer complex attention, story memory, planning, sequencing & motor speed. |
| Infante et al. (2019) | Longitudinal | 175 | 12-29-Baseline: 12-15-Follow-up: 12-29 | 57/43 | Lifetime use during adolescence (+) impairments in inhibitory control & visuospatial functioning. (NC) verbal memory. |
| Scott et al. (2017) | Cross-sectional | 4,585 | 14-21 (Frequent cannabis user Mage: 17.6; Occasional cannabis user Mage: 17.4; Cannabis non-user Mage: 16.4) | 44/56 | Frequent & earlier onset, but not occasional cannabis use (+) executive functioning deficits. |
| Hanson et al. (2010) | Longitudinal | 40 | 15-19-Baseline: 15-19 (Cannabis user Mage: 18.1; Cannabis non-user Mage: 17.4)-Follow-up: 15-19 | 83/17 | Cannabis use poorer (+) verbal learning, verbal working memory & attention accuracy. Verbal learning & verbal working memory deficits improved after three weeks of abstinence. |
| Castellanos-Ryan et al. (2017) | Longitudinal | 295 | 13-20-Baseline: 13-Follow-up: 20 | 100/0 | Bidirectional relationship between cannabis use & short-term & working memory. |
| Meier et al. (2012) | Longitudinal | 1,037 | 13-32-Baseline (Neuropsychological testing): 13-Follow-up (Neuropsychological testing): 38-Cannabis use reporting: 18-32 | 52/48 | Cannabis use (-) in IQ. Cessation of use did not fully restore the impairment. |
| Mokrysz et al. (2016) | Longitudinal | 2,235 | 8-15-IQ score administration: 8, 15-Cannabis use data: 15 | 47/53 | (NC) in IQ or educational performance after adjusting for cigarette use. |
| Meier et al. (2018) | Longitudinal | 1,989 | 5-18-Baseline: 5-12-Follow-up: 18 | 47/53 | Cannabis dependents youth ↓ IQ at ages 12 and 18, but cannabis dependence (**≠)** IQ declines. Executive performance (=) in co-twin pairs at age 18. |
| Jackson et al. (2016) | Longitudinal | Study 1: 789Study2: 2,277 | 9-20-Baseline: 9-10 (Mage: 9.6)-Follow-up: 19-20 (Mage: 19.8)11-18-Baseline: 11 (Mage: 11.8)-Follow-up: 18 (Mage: 18.1) | Study 1:48/52Study 2:49/51 | Lower IQ not observed in cannabis-using twins relative to their non-user co-twin, suggesting involvement of familial factors. |
| Duperrouzel et al. (2019) | Longitudinal | 401 | 14-18-Baseline: 14-17 (Mage: 15.4)-Follow-up: 14-19\* | 55/45 | Cannabis users ↓ performance in decision-making & episodic memory performance at baseline. Cannabis use (+) worsening of immediate episodic memory. |
| Harvey et al. (2007) | Cross-sectional | 70 | 13-18 (Mage: 16.2) | 40/60 | Regular cannabis use (+) impairments in attention, spatial working memory, & learning. |
| Medina et al. (2007a) | Cross-sectional | 65 | 16-18 (Cannabis user Mage: 18.1; Cannabis non-user Mage: 17.9) | 74/26 | Cannabis use (+) poorer complex attention, story memory planning, sequencing & motor speed. |
| Vo et al. (2014) | Cross-sectional | 42 | 16-20 years (Mage: 17.9) | 70/30 | CUD (+) working memory impairments. |
| Padula et al. (2007) | Cross-sectional | 34 | 16-18 (Cannabis user Mage: 18.1; Cannabis non-user Mage: 17.9) | 77/23 | Cannabis use ≠ differences in working memory but (+) ↑ activation in the right basal ganglia & associated with skill-learning. |
| Pope et al. (2003) | Retrospective | 209 | -Early onset user Mage: 36-Late onset user Mage: 44-Non-user control Mage: 40 | 49/51 | Early onset of use (+) poorer cognitive performance. |
| Fontes et al. (2011) | Retrospective | 148 | 18-55 (Early onset user Mage: 30.4; Late onset user Mage: 30.0; Non-user Mage: 27.8) | 68/32 | Early onset of use (+) sustained attention, impulse control & executive function impairments. |
| Noorbakhsh et al. (2020) | Longitudinal | 3826 | 12-17-Baseline: 12.7-Follow-up: 17.7\* | 53/47 | Age of initiation of use (-) spatial working memory deficits over five years (♀ only). |
| Psychopathology |  |  |  |  |  |
| Arseneault et al. (2002) | Longitudinal | 759 | 15-26-Baseline: 15,18-Follow-up: 26 | N/A | Use at age 18 (+) risk for schizophrenia at age 26. |
| Jones et al. (2018) | Longitudinal | 3,328 | -Baseline: 14-19-Follow-up: 19-24\* | N/A | Cannabis use (+) risk of psychotic experiences. |
| Shahzade et al. (2018) | Retrospective | 178 | 18-40 (Mage: 23.9) | 56/48 | Motives for cannabis use (+) risk of schizophrenia spectrum disorder & schizotypal symptom severity. |
| Hanna et al. (2016) | Retrospective | 161 | 15-65 | 48/52 | Adolescent-onset cannabis use (+) better cognitive function in the schizophrenia/schizoaffective subgroup but not in the bipolar psychosis group. |
| French et al. (2015) | Longitudinal | 1,577 | 12-21-Baseline: 16-Follow-up: 18-21 | 57/43 | Early use (-) cortical thickness in ♂ with a high genetic risk for schizophrenia. |
| Albertella et al. (2017) | Longitudinal | 162 | 15-24 (Early onset user Mage: 19.7; Late onset user Mage: 20.7) | 41/59 | Early onset use (+) introvertive anhedonia (♀ only). |
| Hiemstra et al. (2018) | Longitudinal | 497 | 13-20-Baseline: 13-Follow-up: 13-20 | 57/43 | Genetic vulnerability for schizophrenia (+) cannabis use at age 16-20. |
| Kaasbøll et al. (2018) | Cross-sectional | 33,714 | 13-17 | 50/50 | Cannabis use (+) anxiety & depressive symptoms. Although cannabis use was less prevalent among girls, girls reported more anxiety and depressive symptoms compared to boys. |
| McQueeny et al. (2011) | Cross-sectional | 82 | 16-19 (♂ Cannabis user Mage: 17.9; ♀ Cannabis user Mage: 18.2; ♂ Cannabis non-user Mage: 17.7; ♀ Cannabis non-user Mage: 17.9) | 77/23 | Cannabis use (+) larger right amygdala volumes & ↑ anxiety/depressive symptoms (♀ only). |
| Hengartner et al. (2020) | Longitudinal | 4,547 | 19-50-Baseline: 19-20-Follow-up: 20-50 | 48/52 | Age of onset (-) risk of depression in adulthood. |
| Womack et al. (2016) | Longitudinal | 264 | 17-22-Baseline: 17-Follow-up: 20-22 | 100/0 | Cannabis use (+) in later depressive symptoms in those with mild depression. |
| Duperrouzel et al. (2018) | Longitudinal | 401 | 14-18-Baseline: 14-17 (Mage: 15.4)-Follow-up: 15-18 | 56/44 | Levels of early cannabis more (+) persistent self-reported anxiety over time. |
| Assari et al. (2018) | Longitudinal | 681 | 14-19\*-Baseline Mage: 14.9-Follow-up: 15-19\* | 49/51 | Cannabis use (+) depressive symptoms (♂ only). |
| Future Substance Use |
| Degenhardt et al. (2010) | Longitudinal | 1,520 | 13-24-Baseline: 13-15\* (Mage: 14.9)-Follow-up: 24-25 (Mage: 24.1) | 46/54 | Occasional use ↑ risk of developing future alcohol dependence & illicit drug use. |
| Swift et al. (2012) | Longitudinal | 1,756 | 14-29-Baseline: 14.9-17.4-Follow-up: 20-29 | 47/53 | Weekly & daily use ↑ rates of illicit drug use & cigarette smoking, respectively. |
| Scholes-Balog et al. (2016) | Longitudinal | 852 | 12-21-Baseline: 12-19-Follow-up: 21 | 43/57 | Early onset users ↑ cannabis use frequency & substance-use related harms in young adulthood. |
| Jin et al. (2017) | Longitudinal | 712 | 15-41-Baseline: 15-19 (Cannabis user Mage: 17.2; Cannabis non-user Mage: 16.9)-Follow-up: 35-41 | 41/59 | Cannabis use at baseline (+) cigarette smoking & alcohol intake the follow-up. |
| Taylor et al. (2017) | Longitudinal | 5,315 | 13-21-Baseline: 13-18-Follow-up: 21 | N/A | Users ↑ odd of nicotine dependence, harmful alcohol consumption & illicit drug use. |
| Pampati et al. (2018) | Longitudinal | 2,359 | 13-32-Baseline: 13-21-Follow-up: 14-32 | 46/54 | Higher cannabis & alcohol use frequency (+) persistence of cannabis use. |
| Creswell et al. (2015) | Longitudinal | 447 | 12-25-Baseline: 12-18 (Mage: 16.2) | 54/46 | Solitary use (+) more frequent cannabis use & more CUD symptoms in young adulthood. |
| Cassidy et al. (2018) | Longitudinal | 1,313 | Baseline Mage: 18.6 | 45/55 | E-cigarette use (+) initiation of cannabis vaping. Lifetime cannabis & cigarette use (+) e-cigarette use. |
| Solowij et al. (2012) | Cross-sectional | 175 | 16-20 (Mage: 18.3) | 45/55 | Early onset & greater duration of use (+) impairments in decision-making. |
| Lane et al. (2005) | Cross-sectional | 34 | 14-18 (Cannabis user Mage: 16.8; Cannabis non-user Mage: 16.2) | 68/32 | Cannabis users ↓ motivation. |
| Acheson et al. (2015) | Cross-sectional | 28 | Mage: 17.5 | 79/21 | Users ↑ neural response to both wins & losses in the monetary delay task; Differences in connectivity of 1/3rd of total paths analyzed. |

Table 3B: Summaries of cross-sectional, retrospective, and longitudinal imaging studies assessing the potential structural and functional vulnerability outcomes of use of cannabis by adolescents. \* = estimation; (↑) = increase; (↓) = decrease; (=) = same as control; (NC) = no change; (+) = positive association; (-) = negative association; (≠) = no association; male = ♂; female = ♀; Mage = mean age.

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| --- | --- | --- | --- | --- | --- |
| Author | Study Type | N | Age | Gender % (♂/♀) | Findings |
| Functional |
| Behan et al. (2014) | Cross-sectional | 35 | 14-19 (Cannabis user Mage: 16.5; Cannabis non-user Mage: 16.1) | 94/6 | Cannabis use (-) inhibitory control, which (+) aberrant activity between bilateral inferior parietal lobule & the left cerebellum. |
| Tapert et al. (2007) | Cross-sectional | 33 | 16-18.9 (Cannabis user Mage: 18.1; Cannabis non-user Mage: 17.9) | 73/27 | Cannabis use (≠) differences in inhibitory control task performance but (+) brain processing. |
| Abdullaev et al. (2010) | Cross-sectional; Retrospective | 28 | Mage: 19.6 | 71/29 | Adolescent onset chronic cannabis use (+) impairments in executive attention & ↑ activation within the right PFC in young adults. |
| Camchong et al. (2017) | Longitudinal | 65 | 10-22\*-Baseline: 10-21-Follow-up: 11-22\* | 57/43 | CUD (-) functional connectivity between caudal ACC with the DLPFC & OFC across time. Functional connectivity between caudal ACC & OFC at baseline (-) cannabis use, which (-) IQ & slower cognitive function |
| Jager et al. (2010) | Cross-sectional | 45 | 13-19 (Cannabis user Mage: 17.2; Cannabis non-user Mage: 16.8) | 100/0 | Cannabis users = associative learning & working memory tasks; ↑ activity levels in the prefrontal regions when the working memory task was novel. |
| Jacobsen et al. (2004) | Cross-sectional | 21 | -Cannabis user Mage: 17.4-Tobacco smoker Mage: 17.1-Non-smoker Mage: 16.8 | 38/62 | Cannabis use (+) impairments in sustained attention & working memory; failure to reduce activity in right hippocampus during working memory task. |
| Tervo-Clemmens et al. (2018) | Longitudinal | 75 | 14-28-Baseline: 14-22-Follow-up: 28 | 46/64 | Age of onset of use (-) reaction times & ↓ activation in the posterior parietal cortex. |
| Spechler et al. (2015) | Cross-sectional | 140 | Mage: 14.7 | 65/35 | Cannabis use (+) greater sensitivity to angry faces as indicated by ↑ reactivity in the bilateral amygdala. |
| Aloi et al. (2018) | Cross-sectional | 97 | 14-18 (Mage: 16.1) | 62/38 | AUD, nut not CUD, symptom severity (+) amygdala activity to emotional stimuli. |
| Subramaniam et al. (2018) | Cross-sectional | 74 | 14-20 (Cannabis user Mage: 18.0; Cannabis non-user Mage: 17.1) | 80/20 | Users exhibited alterations in OFC connectivity, (+) depression & anxiety symptoms. |
| Lichenstein et al. (2017) | Longitudinal | 158 | Adolescent cannabis use data collection: 14-19-fMRI and substance use data collection: 20-Psychological outcomes data collection: 22 | 100/0 | Escalating cannabis use (+) negative functional connectivity between the nucleus accumbens & medical PFC, (+) higher depressive symptoms & anhedonia. |
| De Bellis et al. (2013) | Cross-sectional | 56 | 13-17 | 100/0 | CUD (+) hyperactivation in brain regions implicated in risky & uncertain decision-making. |
| Jager et al. (2013) | Cross-sectional | 45 | 13-19 (Cannabis user Mage: 17.2; Cannabis non-user Mage: 16.8) | 100/0 | Cannabis users = in monetary incentive delay task assessing reward-related brain function; striatal hyperactivity during the anticipatory stages of reward. |
| Nestor et al. (2019) | Cross-sectional | 36 | -Cannabis user Mage: 16.50-Cannabis non-user Mage: 16.11 | 94/6 | Cannabis dependent adolescents ↑ performance & ↑ global connectivity during the anticipatory stages of monetary incentive delay task. |
| Structural |  |  |  |  |  |
| Medina et al. (2010) | Cross-sectional | 32 | 16-18 (Mage: 18.0) | 68/31 | Users ↑ inferior posterior vermis & larger posterior cerebellar vermis volumes, which in turn (+) poorer executive functions. |
| Medina et al. (2009) | Cross-sectional | 32 | 16-18 (Mage: 18.0) | 69/31 | Users ↑ (♂) & ↓ (♀) PFC volumes. PFC volume (-) better executive functioning among users. |
| Churchwell et al. (2010) | Cross-sectional | 36 | 16-19 (Cannabis abuser Mage: 17.7; Cannabis non-abuser Mage: 17.2) | 78/22 | Cannabis use (-) right medial orbital PFC volume. Medial orbital PFC volume (+) age of first use. |
| Ashtari et al. (2011) | Cross-sectional | 28 | 18-20 (Mage: 18.9) | 100/0 | Heavy use (+) smaller left hippocampus volumes. (NC) in bilateral amygdala volume. |
| Weiland et al. (2015) | Cross-sectional | Adults: 68Youth: 100 | Adolescent: 14-18 (Daily cannabis user Mage: 16.7; Cannabis non-user Mage: 16.8)-Adult: 18-53 (Daily cannabis user Mage: 27.4; Cannabis non-user Mage: 27.6) | Adults: 77/23Youth: 55/45 | (NC) in accumbens, amygdala, hippocampus, or cerebellum volumes. |
| Scott et al. (2019) | Cross-sectional | 781 | 14-22 (Frequent cannabis user Mage: 18.5; Occasional cannabis user Mage: 18.1; Cannabis non-user Mage: 17.0) | 43/57 | (NC) in global or regional brain volumes, cortical thickness, and gray matter density. |
| Becker et al. (2015) | Longitudinal | 46 | 18-22-Baseline: 18-20 (Mage: 19.3\*)-Follow-up: 20-22 | 70/30 | Cannabis use (-) longitudinal growth of FA in the left superior longitudinal fasciculus, left corticospinal tract, right anterior thalamic radiation & poor verbal learning performance. |
| Ashtari et al. (2009) | Cross-sectional | 28 | 17-21 (Mage: 18.9) | 100/0 | Heavy cannabis history ↓ FA, as well as ↑ radial diffusivity & increased trace in frontotemporal white matter circuits. |
| Epstein and Kumra (2015) | Longitudinal | 79 | -Baseline: 10-23 (CUD Mage: 16.4; Non-CUD Mage: 17.0)-Follow-up: 12-25 | 54/46 | CUD (-) normative loss of cortical thickness in the heteromodal association cortex. |
| Orr et al. (2019) | Longitudinal | 92 | 14-16-Baseline: 14-Follow-up: 16 | 75/25 | Users ↑ GMV in the bilateral medial temporal lobes, bilateral posterior cingulate, lingual gyri, & cerebellum. |
| Wilson et al. (2000) | Retrospective | 57 | 19-48 (♂ Early onset cannabis user Mage: 31.5; ♀ Early onset cannabis user Mage: 27.9; ♂ Late onset cannabis user Mage: 33.2; ♀ Late onset cannabis user Mage: 33.1) | 56/44 | Age of onset of use (+) whole brain & percent cortical gray matter, (-) percent white matter volume. |
| Meier et al. (2019) | Longitudinal | 181 | 13-36-Baseline: 13-19-Follow-up: 30-36 | 100/0 | Cannabis use (≠) structural differences in subcortical or cortical brain regions. |
| Kumra et al. (2012) | Cross-sectional | 115 | 10-21 (Early onset schizophrenia with CUD Mage: 17.5; CUD Mage: 16.6; Early onset schizophrenia Mage: 16.5; Control Mage: 16.2) | 53/47 | Age of onset schizophrenia & CUD (-) GMV in the left superior parietal cortex. |
| Medina et al. (2007b) | Cross-sectional | 32 | 16-18 (Mage: 18) | 72/28 | Cannabis use (+) depressive symptoms, (-) white matter volume; white matter volume (-) depressive symptoms. |
| Cheetham et al. (2012) | Longitudinal | 121 | 12-16-Baseline: 12 (Mage: 12.7)-Follow-up: 16 (Mage: 16.5) | 51/49 | Smaller OFC volumes at age 12 ↑ initiation of cannabis use by age 16. |

Table 4: Summaries of cross-sectional, retrospective, and longitudinal studies assessing the potential cognitive, behavioral, psychopathological, and future substance use vulnerability outcomes of use of opioids by adolescents (↓) = decrease; (+) = positive association; male = ♂; female = ♀; Mage = mean age.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Author | Study Type | N | Age | Gender % (♂/♀) | Findings |
| **Cognition** |
| Vo et al. (2014) | Cross-sectional | 42 | 16-20 (Mage: 18.7) | 70/30 | Opioid use disorder ↓ working memory. |
| **Psychopathology** |
| Edlund et al. (2015) | Cross-sectional | 112,600 | 12-17 (Mage: 14.5) | 51/49 | Opioid use (+) major depression. |
| Subramaniam and Stitzer (2009) | Cross-sectional | 94 | 14-18 (Mage: 17) | 100/0 | Heroin & prescription opioid use (+) comorbid psychiatric disorders, multiple SUD, ADHD, manic episodes, criminal behavior, major depressive episode. |
| Subramaniam et al. (2009) | Cross-sectional | 168 | 14-18 (Mage: 16.75) | 61/39 | Opioid dependence (+) substance use, depressive symptoms, & decreased academic success. |
| **Future Substance Use** |
| Cerda et al. (2015) | Cross-sectional | 223,534 | 12-21 (Mage: 16.5) | 51/49 | Misuse of prescription opioids (+) future heroin use. |
| Miech et al. (2015) | Longitudinal | 6,220 | 17-23Baseline: 17-19Follow-up: 23 | N/A | Legitimate use of prescription opioids (+) risk of future misuse. |

Table 5A: Summaries of cross-sectional, retrospective, and longitudinal studies assessing the potential cognitive, behavioral, psychopathological, and future substance use vulnerability outcomes of co-use of substances by adolescents. AC = alcohol and cannabis co-use; AN = alcohol and nicotine products co-use; all = co-use of three or more substances; \* = estimation; (↑) = increase; (↓) = decrease; (+) = positive association; male = ♂; female = ♀; Mage = mean age.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Author | Study Type | N | Age | Gender % (♂/♀) | Findings |
| Cognition |
| Jacobus et al. (2015)AC | Longitudinal | 108 | 16-19 (Mage: 17.8 (baseline), 20.8 (follow-up)) | 65/35 | Co-use ↓ complex attention, memory, processing speed, & visuospatial functioning. |
| Mahmood et al. (2010)AC | Cross-sectional | 130 | 15-19 (Mage: 17.8) | 75/25 | Heavy alcohol users ↓ verbal learning & memory during hangover. Deficits not seen in co-users. |
| Morin et al. (2019)AC | Longitudinal | 3,826 | 12-17 (Mage: 12.7 (baseline), 16.7 (follow-up)) | 53/47 | Cannabis but not alcohol ↓ working memory & inhibitory control (short-term); ↓ perceptual reasoning & delayed memory recall (long-term). |
| Terry-McElrath et al. (2014)AC | Cross-sectional | 72,053 | 17-19 | 47/53 | Simultaneous use ↑ risk for unsafe driving vs. concurrent or alcohol only. |
| Winward et al. (2014)AC | Cross-sectional | 128 | 16-18 (Mage: 17.8) | 65/35 | Following abstinence, heavy co-users ↓ working memory vs. individual users. |
| **Psychopathology** |  |  |  |  |  |
| Boys et al. (2003)all | Cross-sectional | 2,624 | 13-15 (Mage: 14) | 50/50 | Tobacco, alcohol & cannabis (+) additive risk for depressive disorders. Except for cannabis & alcohol, all co-use (+) risk for any psychiatric disorder. |
| Matuszka et al. (2016)AN | Cross-sectional | 944 | 14-16 (Mage: 15.04) | N/A | Co-use additively ↑ physical aggression. |
| **Future Substance Use** |
| Briere et al. (2011)AC | Longitudinal | 6,589 | 12-17 (Mage: 12.8 (baseline), 15.5 (follow-up)) | 48/52 | Simultaneous use (+) future substance-related issues vs. concurrent use. |
| Green et al. (2016) | Longitudinal | 608 | 6-25Baseline: 6Follow-up: 19-25 | 54/46 | Co-use (+) future negative outcomes in young adulthood in areas of substance use, graduation, criminal record, income & employment. |
| Grucza and Bierut (2006)AN | Cross-sectional | 74,836 | 12-20 (Mage: 15\*) | 51/49 | Past-year smokers drank more alcohol than non-smokers & ↑ risk for AUD compared to non-smokers who drank equivalent amounts. |
| Patrick et al. (2018)AC | Cross-sectional | 84,805 | 17-19 | 52/48 | Simultaneous use (+) level of illicit substance use other than cannabis, truancy, & nights out. |
| Rubinstein et al. (2014)CN | Cross-sectional | 165 | 13-17 (Mage: 16.1) | 48/52 | Cannabis use (+) reported nicotine addiction among adolescent smokers. |
| Schmid et al. (2007)AN | Cross-sectional | 384 | 14-16 (Mage: 14.9 (baseline)) | 48/52 | Alcohol & tobacco users ↑ alcohol use, initiated alcohol use at a younger age, ↑ cannabis use, had ↑ nicotine dependence scores & novelty seeking vs. alcohol users. |

Table 5B: Summaries of cross-sectional, retrospective, and longitudinal imaging studies assessing the potential structural and functional vulnerability outcomes of co-use of substances by adolescents. AC = alcohol & cannabis co-use; AN = alcohol & nicotine products co-use; all = co-use of three or more substances. \* = estimation; (↑) = Increase; (↓) = decrease; (=) = same as control; (NC) = no change; (+) = positive association; (-) = negative association; male= ♂; ♀= female; Mage = mean age.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Author | Study Type | N | Age | Gender % (♂/♀) | Findings |
| Structural |
| Bava et al. (2009) AC | Cross-sectional | 72 | 16-19 (Mage: 17.9) | 28/72 | Co-users ↓ FA in 10 regions, ↑ FA in three regions, ↓ mean diffusivity in one region, & ↑ mean diffusivity in one region. |
| Bava et al. (2010) AC | Cross-sectional | 72 | 16-19 (Mage: 17.9) | 28/72 | Co-users ↓ FA in temporal brain areas, which was (-) attention, working memory & speeded processing. ↑ FA in occipital regions (+) working memory & complex sequencing. |
| Bava et al. (2013)AC | Longitudinal | 92 | 16-20 (Mage: 18.1 (baseline), 19.6 (follow-up)) | 68/32 | Co-users ↓ white matter integrity in seven tracts. More alcohol use ↓ integrity in right & left superior longitudinal fasciculi. |
| Infante et al. (2019)AC | Longitudinal | 69 | 12-21 (Mage: 13.7 (baseline), 19.2 (follow-up)) | 56.5/43.5 | Alcohol only ↓ OFC grey matter surface area. |
| Jacobus et al. (2009)AC | Cross-sectional | 42 | 16-19 (Mage: 17.9) | 86/14 | Binge drinking ↓ FA in eight regions. Co-users ↑ FA vs. binge drinkers in four regions. |
| Jacobus et al. (2013a)AC | Longitudinal | 54 | 16-22 (Mage: 17.9 (baseline), 20.9 (follow-up)) | 59/41 | Binge drinkers & co-users had similarly ↓ FA. |
| Jacobus et al. (2013b)AC | Longitudinal | 16 | 16-22(Mage: 17.9 (Baseline), 20.9 (follow-up)) | N/A | Teens who would go on to initiate co-use showed FA > or = to alcohol only initiation; co-use initiation ↓ FA. |
| Jacobus et al. (2014)AC | Cross-sectional;Retrospective | 54 | 15-18 (Mage: 17.5) | 72/28 | Co-use ↑ cortical thickness in left entorhinal cortex. Cannabis use ↓ cortical thickness in frontal & temporal lobes. Alcohol use ↑ cortical thickness in all regions. |
| Jacobus et al. (2015)AC | Longitudinal | 68 | 16-22Baseline: 16-19 (Mage: 17.9 (Baseline), 21 (follow-up)) | 70/30 | Co-use ↑ cortical thickness in 23 regions. Cannabis ↑ thickness; alcohol ↓ thickness. |
| Jacobus et al. (2016)AC | Longitudinal | 69 | 12-21 (Mage: 13.7 (baseline), 19.2 (follow-up)) | 56.5/43.5 | Alcohol initiators & controls ↑ cortical thickness at baseline. Larger decreases in thickness observed in alcohol initiators & controls vs. co-use initiators. |
| Medina et al. (2007c)AC | Cross-sectional | 63 | 15-18 (Mage: 17.3) | 65/35 | Alcohol users ↑ right > left asymmetry & ↓ left hippocampal volume. Cannabis ↑ left > right asymmetry & ↑ left hippocampal volume. Co-users (NC) in symmetry or volume. |
| **Functional** |  |  |  |  |  |
| Claus et al. (2018)AC | Cross-sectional | 189 | 14-18 (Mage: 16.2) | 75/25 | Co-use ↓ BOLD response in thalamus, insula & striatum during balloon analog risk-taking task. |
| Karoly et al. (2015)all | Cross-sectional | 239 | 14-18 (Mage: 15.9) | 65/35 | Tobacco use ↓ BOLD response in nucleus accumbens during monetary incentive delay task. (NC) in tobacco+cannabis/ tobacco+cannabis+alcohol. |
| Schweinsburg et al. (2005)AC | Cross-sectional | 49 | 15-17 (Mage: 16.7) | 67/33 | Alcohol+cannabis use disorder ↓ BOLD activation in inferior frontal & temporal regions & ↑ activation in medial frontal regions vs. AUD |
| Schweinsburg et al. (2011)AC | Cross-sectional | 74 | 16-18 (Mage: 18) | 80/20 | Binge drinking or cannabis use ↑ BOLD response in bilateral frontal regions during verbal-paired associates encoding task. Co-users (=) non-users. |

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