**Supplementary Material**

**Method**

**Measures**

**Family risk index.** The measure of family adversity includes information on family status (intact or not), both parents’ educational level, occupational prestige, and their age at the birth of their first child. For each item, a score of 1 was given to those below the 30th percentile of the complete sample, and a score of 0 was given to those above the 30th percentile (an intact family status was given a score of 0), with higher scores indicating greater adversity.

**Academic Achievement.** Academic achievement was assessed annually from 13 to 15 years using teacher ratings of adolescent’s overall school performance (including math, reading and writing). Specifically, teachers were asked to compare the performance of each child with the average performance of his or her schoolmates on a 5-point Likert scale (1 = clearly under average, 3=average, 5=clearly above average). The teachers were asked to rate the adolescents by the end of the school year so they could base their ratings on several previous assessments of the adolescent’s achievement relative to that of their classmates during that year. Academic achievement from 13to 15 years was averaged to create an academic achievement score.

**Data preparation and Statistical Analysis.** Although all 294 participants who completed the neurocognitive battery at age 20, had a verbal IQ estimate at 13 years (i.e., a sentence completion task), only a subset of 112 participants also completed the vocabulary subtest of the Wechsler Intelligence Scale for Children-Revised (Wechsler, 1974) at 15 years. Because the age 15 years verbal IQ estimate based on the vocabulary subtest score was obtained after cannabis use onset for some participants, it only served to validate use of the age 13 years verbal IQ estimate based on the sentence completion task as a baseline measure to compute change scores in the verbal IQ estimate across adolescence. That is, analyses using the IQ vocabulary subtest at 20 years were run twice and compared: 1) with change scores using the standardized sentence completion task score at 13 as baseline and standardized vocabulary score at age 20, and 2) with change scores using the raw vocabulary scale score at 15 years as baseline and raw vocabulary scale score at 20 years. Results using either of these change scores were equivalent. Moreover, to further validate the sentence completion score at 13, IQ Vocabulary subtest scores assessed at 12 years, which were available for 53 participants, where found to correlate strongly with the sentence completion at 13 years (vocabulary at r=.71).

**Results**

**Preliminary analysis: Unconditional latent growth model of cannabis use frequency**

A linear growth function fit the cannabis-use frequency data adequately (χ2 =16.7; DF=5; CFI= .95; RMSEA=.08; SRMR=.08). Although a quadratic model fit the data better (χ2 =0.97; DF=1; CFI=1.00; RMSEA=.00; SRMR=.01), it resulted in latent variables with negative variance, which suggests that the variance was not better explained with the addition of a quadratic function, but that the growth may not be completely linear across all time points. Thus, a final growth model was conducted where growth was assumed to be linear across the first three time points (14 to 16 years), but left to be freely estimated for the last time point (17 years; see Figure 1). The last growth parameter was chosen to be freely estimated because the means across time suggested that the mean increase from 16 to 17 years was slightly lower than for other time points. This model fit the data better than the linear model (χ2 =10.6; DF=4; CFI= .97; RMSEA=.07; SRMR=.06) and showed that growth between time-points 3 (16 years) and 4 (17 years) was indeed smaller than at other time points (with the freely estimated loading resulting in 2.40 vs. 3.00). Growth curve factor means (intercept= 1.29; slope= 0.48) were significantly different from zero at p<.001, and showed that there was an overall tendency for CU frequency to increase from 14 to 17 years. The growth curve factor variances were also significant at p<.01 (intercept= 0.61; slope= 0.39), indicating that there was significant individual variability in the mean level of CU at 14 years and its pattern of change over time. Correlations between the latent factors showed that CU at age 14 years (intercept) did not correlate significantly with the increase of cannabis use frequency across adolescence (slope, r=.32, p=.15).

**Supplementary results**

Because the Card Playing Task (CAPT) assessed not only trial-and-error learning (and rule induction), which is also captured by the conditional association task, but also reward/punishment processing, a regression analysis was conducted to test whether effects on the Card Playing Task could be partly explained by the effects on the conditional association task. When adjusting for change in conditional association learning (which was significantly associated with change in the CAPT; β=.21, p=.001), cannabis use frequency at age 14 (intercept factor) was still significantly associated with less improvement on the CAPT (β=-.25, p=.001; vs β=-.28 when not controlling for change in conditional association), suggesting that early frequent cannabis use may interfere not only with learning by trial and error, but also with reward/punishment processing.

**Cannabis-using groups and cognitive performance.**

In order to compare findings from continuous analyses with those obtained with group based analyses, cannabis use groups were created based on participants’ cannabis use frequency across 14 to 17 years. The following six groups of CU were identified: 1) No use (n=150, 51% of sample); 2) Experimental or occasional use before 17 years (n=18, 6%; these adolescents used cannabis once or twice before the age of 17, at one time point only); 3) Cannabis use from 17 years (n=21, 7%); 4) Cannabis use from 16 years (n=32, 11%); 5) Cannabis use from 15 years (n=46, 16%); and 6) Cannabis use from 14 years (n=27, 9%). Adolescents who experimented with cannabis only occasionally (1 to 2 times) at only one time point were assigned to the “experimental or occasional use before 17 years” group. See Table S2 for additional characterization of CU across adolescence by group and table S3 for change in cognitive function from 13/14 years to 20 years by group.

Univariate Analyses of Variance (ANOVAs) were used to examine the association between these cannabis using groups and change in cognitive function. Results were similar to those reported in the main text of manuscript. That is, significant differences across groups were found only for the verbal IQ, conditional association task and the card playing tasks, and showed that most cannabis using groups differ significantly from non-users on verbal IQ, only adolescents who start using cannabis before the age of 16 differ from non-users on the conditional association task, and only adolescents who start using cannabis before 15 years differ significantly from non-users on the card playing task (see supplementary Table S.3).

**References**

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Table S.1. Correlations between neurocognitive variables in early adolescence and early adulthood

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
| 1 | Verbal IQ at 13 | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 2 | Number random at 13 | .38\*\* | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 3 | DS Forward at 13 | .51\*\* | .29\*\* | 1 |  |  |  |  |  |  |  |  |  |  |  |  |
| 4 | DS back at 13 | .38\*\* | .32\*\* | .63\*\* | 1 |  |  |  |  |  |  |  |  |  |  |  |
| 5 | SOP at 14 | .28\*\* | .38\*\* | .30\*\* | .28\*\* | 1 |  |  |  |  |  |  |  |  |  |  |
| 6 | PAL at 14 | .54\*\* | .43\*\* | .57\*\* | .43\*\* | .27\*\* | 1 |  |  |  |  |  |  |  |  |  |
| 7 | Conditional at 14 | .33\*\* | .55\*\* | .45\*\* | .45\*\* | .49\*\* | .52\*\* | 1 |  |  |  |  |  |  |  |  |
| 8 | CAPT at 13 | -.02 | .13\* | -.04 | -.04 | .33\*\* | -.03 | .09 | 1 |  |  |  |  |  |  |  |
| 9 | Verbal IQ at 20 | .56\*\* | .37\*\* | .35\*\* | .28\*\* | .39\*\* | .61\*\* | .36\*\* | -.15\* | 1 |  |  |  |  |  |  |
| 10 | Number random at 20 | .22\*\* | .45\*\* | .30\*\* | .41\*\* | .35\*\* | .36\*\* | .43\*\* | -.21\*\* | .25\*\* | 1 |  |  |  |  |  |
| 11 | DS Forward at 20 | .37\*\* | .11 | .72\*\* | .71\*\* | .29\*\* | .49\*\* | .36\*\* | .16\*\* | .26\*\* | .31\*\* | 1 |  |  |  |  |
| 12 | DS back at 20 | .27\*\* | .34\*\* | .54\*\* | .68\*\* | .23\*\* | .47\*\* | .29\*\* | -.03 | .32\*\* | .32\*\* | .57\*\* | 1 |  |  |  |
| 13 | SOP at 20 | .43\*\* | .46\*\* | .41\*\* | .37\*\* | .55\*\* | .48\*\* | .54\*\* | .14\* | .48\*\* | .37\*\* | .33\*\* | .30\*\* | 1 |  |  |
| 14 | PAL at 20 | .34\*\* | .27\*\* | .48\*\* | .31\*\* | .20\*\* | .70\*\* | .41\*\* | -.06 | .43\*\* | .24\*\* | .37\*\* | .36\*\* | .33\*\* | 1 |  |
| 15 | Conditional at 20 | .29\*\* | .32\*\* | .41\*\* | .27\*\* | .29\*\* | .48\*\* | .52\*\* | .03 | .26\*\* | .33\*\* | .21\*\* | .25\*\* | .38\*\* | .34\*\* | 1 |
| 16 | CAPT at 20 | -.07 | .01 | -.07 | .03 | .07 | -.06 | .03 | .25\*\* | .00 | .01 | -.07 | -.06 | .07 | -.04 | .07 |

Note:DS: Digit Span; SOP: Self-Ordered Pointing; PAL: Paired Associates Learning; CAPT: Card Playing Task \* p<.05, \*\* p<.01.

Table S.2. Correlations between neurocognitive variables and covariates

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Age | Family adversity | Other drug use 20 | Cannabis use 20 | Tobacco use 20 | Academic achieve 13-15 | High-school graduation | ADHD 13-15y | CD 13-15y | Alcohol use 13-17y | Tobacco use 13-17y |
| Verbal IQ at 13 | -.02 | -.21\*\* | .01 | .01 | -.14\* | .26\*\* | .42\*\* | -.29\*\* | -.27\*\* | .20\*\* | -.09 |
| Number random at 13 | -.02 | -.23\*\* | -.01 | -.07 | -11 | .33\*\* | .32\*\* | -.32\*\* | -.27\*\* | .02 | -.13\* |
| DS Forward at 13 | -.08 | -.16\*\* | -.02 | .14\* | -.09 | .31\*\* | .33\*\* | -.20\*\* | -.20\*\* | .16\*\* | -.06 |
| DS back at 13 | -.14\* | -.12\* | .05 | -.02 | -.06 | .32\*\* | .31\*\* | -.21\*\* | -.18\*\* | .20\*\* | -.06 |
| SOP at 14 | .04 | -.13\* | -.12\* | .12\* | -.14\* | .34\*\* | .32\*\* | -.23\*\* | -.19\*\* | .04 | -.17\*\* |
| PAL at 14 | -.14\* | -.41\*\* | .01 | -.10 | -.17\*\* | .40\*\* | .52\*\* | -.34\*\* | -.37\*\* | .08 | -.15\* |
| Conditional at 14 | .12\* | -.35\*\* | -.04 | -.08 | -.17\*\* | .36\*\* | .36\*\* | -.27\*\* | -.30\*\* | .16\*\* | -.100 |
| CAPT at 13 | -.07 | -.16\*\* | -.12\* | -.02 | -.06 | .16\*\* | .10 | -.07 | -.06 | .03 | -.01 |
| Verbal IQ at 20 | -.08 | -.44\*\* | .05 | -.04 | -.22\*\* | .37\*\* | .61\*\* | -.45\*\* | -.40\*\* | .05 | -.18\*\* |
| Number random at 20 | -.05 | -.20\*\* | -.04 | -.06 | -.08 | .19\*\* | .29\*\* | -.17\*\* | -.18\*\* | .00 | -.14\* |
| DS Forward at 20 | -.05 | -.15\* | .05 | .01 | -.02 | .24\*\* | .23\*\* | -.10 | -.08 | .17\*\* | .00 |
| DS back at 20 | -.11\* | -.20\*\* | .01 | -.08 | -.10 | .34\*\* | .32\*\* | -.267\*\* | -.21\*\* | .13\* | -.10 |
| SOP at 20 | -.13\* | -.29\*\* | -.02 | -.11\* | -.17\*\* | .33\*\* | .44\*\* | -.36\*\* | -.36\*\* | .01 | -.22\*\* |
| PAL at 20 | -.08 | -.25\*\* | .04 | -.01 | -.14\* | .28\*\* | .39\*\* | -.22\*\* | -.30\*\* | -.04 | -.09 |
| Conditional at 20 | -.01 | -.13\* | -.06 | -.06 | -.13\* | .27\*\* | .27\*\* | -.19\*\* | -.27\*\* | -.10 | -.20\*\* |
| CAPT at 20 | .02 | -.08 | -.17\*\* | -.06 | .12\* | .06 | .01 | -.03 | -.04 | .02 | .01 |

Note:DS: Digit Span; SOP: Self-Ordered Pointing; PAL: Paired Associates Learning; CAPT: Card Playing Task \* p<.05, \*\* p<.01.

Table S.3. Cannabis use indicators by adolescent cannabis use groups based on age of onset and frequency of use.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Cannabis Use groups | | | | | |
|  | No use | Experimental use before 17 | Cannabis use from 17 | Cannabis use from 16 | Cannabis use from 15 | Cannabis use from 14 |
|  | N=150 | N=18 | N=21 | N=32 | N=46 | N=27 |
| Cannabis Freq 14, mean | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 3.22 |
| Cannabis Freq 15, mean | 0.00 | 0.29 | 0.00 | 0.00 | 2.71 | 3.46 |
| Cannabis Freq 16, mean | 0.00 | 1.36 | 0.00 | 2.25 | 3.36 | 4.62 |
| Cannabis Freq 17, mean | 0.00 | 0.00 | 2.38 | 3.63 | 3.55 | 4.23 |
| Cannabis Freq 20, mean± | 0.87 | 2.07 | 1.90 | 1.87 | 1.64 | 2.52 |
| Cannabis Use 20 prevalence % (n) | 34 (52) | 77 (14) | 67 (14) | 69 (22) | 57 (26) | 100 (27) |

Note: freq: frequency; Cannabis use frequency rated on the seven point scale: 0=no use, 1=used once or twice, 2=3 to 5 times, 3=6 to 9 times, 4=10 to 19 times, 5=20 to 39 times, 6=40 or more times; ±rated on a four point scale: 0=never, 1=used once or twice, 2=often, 3=very often.

Table S.4. Change in cognitive performance at 20 years (adjusted standardized scores) by adolescent cannabis using groups

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Cannabis Use groups by age of onset and frequency of use | | | | | | |  |  |
|  | No use | Experimental use before 17 | Cannabis use from 17 | | Cannabis use from 16 | Cannabis use from 15 | Cannabis use from 14 |  | |
|  | N=150 | N=18 | N=21 | | N=32 | N=46 | N=27 | F statistic | |
|  | | | |
| Vocabulary┼, correct | 0.219 | 0.058 | -0.274a | | -0.434a | -0.249a | -0.112a | **3.29, p=.007** | |
| Number randomization, trials | 0.008 | 0.081 | 0.055 | | -0.101 | -0.136 | 0.209 | 0.47, p=.799 | |
| DS Forward, correct | -0.024 | -0.458 | 0.172 | | -0.143 | 0.043 | 0.400 | 1.94, p=.088 | |
| DS back, correct | -0.022 | 0.298 | 0.129 | | -0.049 | -0.007 | -0.102 | 0.48, p=.794 | |
| SOP, errors | -0.056 | -0.314 | 0.118 | | -0.040 | 0.177 | 0.177 | 1.09, p=.365 | |
| PAL, correct | 0.040 | 0.128 | -0.331 | | 0.042 | 0.091 | -0.256 | 1.11, p=.358 | |
| Conditional Association, errors | -0.104 | -0.166 | -0.317 | | -0.036 | 0.456a | 0.201a | **3.05, p=.011** | |
| CAPT, cards played | 0.077 | -0.056 | -0.242 | | -0.246 | -0.204 | 0.433a | **2.32, p=.031** | |

Note:DS: Digit Span; SOP: Self-Ordered Pointing; PAL: Paired Associates Learning; CAPT: Card Playing Task; Scores presented in table are mean change scores from early adolescence to 20 years (presented in SD units), adjusting for age at testing, family adversity, academic achievement 13-15 years, verbal IQ at 13 and concurrent cannabis, alcohol, stimulant and tobacco use frequency at 20 years; these change scores can be interpreted as effect sizes, with values of 0.20, 0.50 and 0.80 reflecting small, medium and large effects. ┼ These IQ change scores were calculated by standardizing the sentence completion task (verbal IQ) at 13 years (z-scores) and subtracting it from standardized (z-scored) vocabulary scores at 20 years. Analyses using change scores computed using the vocabulary subtest at 15 years as baseline scores were equivalent to those reported here (differing only by a few decimals), with analyses yielding equivalent results; Letter “a” denotes a significant difference from no use group at p<.05.

Table S.5. Concurrent association (correlations) between neurocognitive function and substance use at 20 years.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Cannabis use | Stimulant Use | Drunkenness | Tobacco Use |
| Vocabulary, correct | -.04 | .05 | -.07 | **-.22** |
| Number randomization, trials | -.06 | -.04 | .08 | -.08 |
| DS Forward, correct | .01 | .05 | **.17** | -.02 |
| DS back, correct | -.08 | .01 | .04 | -.10 |
| SOP, errors | **.11** | .02 | .00 | **.17** |
| PAL, correct | -.01 | .04 | .03 | **-.14** |
| Conditional Association, errors | .06 | .06 | .04 | **.13** |
| CAPT, cards played | .06 | **.17** | .09 | **-.12** |

Note: DS: Digit Span; SOP: Self-Ordered Pointing; PAL: Paired Associates Learning; CAPT: Card Playing Task; numbers in bold indicate significant at level of p<.05