Substance abuse and comorbid problems in adolescents with mild intellectual disability or borderline intellectual functioning.

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Master Science Thesis

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Preface and acknowledgements

Before you lies my major research thesis “Substance abuse and comorbid problems in adolescents with mild intellectual disability or borderline intellectual functioning”, which has been written to fulfil the graduation requirements of the Research Master Behavioural Science at Radboud University. Previous job experiences in research and social work had made me determined to contribute my research efforts for the benefit of vulnerable target groups. Because of that I was, and still am, very grateful for getting the opportunity to perform my research at the Research & Development department at Pluryn, a care facility for children, adolescents, and adults with complex behavioural problems in the Netherlands. A team of scientist practitioners there had developed two intervention programmes for adolescents with substance use problems and mild intellectual disability or borderline intellectual functioning. It was both instructive and exciting for me to able to study the effects of these interventions and the nature of substance use problems in a team where clinical practice and innovative research come together nicely.

I would like to express my gratitude to all Research & Development colleagues at Pluryn who contributed to this thesis to a greater or lesser extent. In particular, I would like to thank my supervisors at Pluryn, Roy Otten and Evelien Poelen, for their confidence in me; their excellent guidance, advice, feedback, and support during this project—from the start until the end—truly meant a lot to me. Finally, I wish to thank Robert Didden for his constructive feedback to the thesis.

I hope you will enjoy reading my major research thesis.

Nijmegen, June 2019 Daan Hulsmans

Abstract

Adolescents with behavioural problems and mild intellectual disability or borderline intellectual functioning (MID-BIF) are at increased risk for problematic substance use (SU) and developing substance use disorder (SUD). Two interventions that targeted personality risk profiles to reduce SU and comorbid problems in MID-BIF adolescents were examined, each with a different approach: a quasi-experiment (study 1, $N = 66$) and a single-case study with daily diary sampling (study 2, 75 days). Intervention effects on- and interrelatedness between SU, affect, behavioural problems were examined to assess *if* and *how* SU changes over time. Both studies demonstrate intervention effectiveness in reducing SU frequency, but not in comorbid problems. Whereas study 1 does not show interactions between SU and comorbid problems, study 2 demonstrates that SUD in an MID-BIF adolescent is a complex dynamical system of continuously interacting affective states and behaviours, in which identifiable early warning signals precede sudden SU improvements or relapse.

Keywords: substance use, substance use disorder, intellectual disability, adolescent, intervention studies, complex systems.

Substance use disorder (SUD) among adolescents with mild intellectual disability or borderline intellectual functioning (MID-BIF; IQ 50-85, American Psychiatric Association, 2013) and comorbid behavioural problems increasingly concerns both scientists and practitioners (Carroll Chapman & Wu, 2012; van Duijvenbode et al., 2015). Compared to adolescents without MID-BIF, those adolescents *with* MID-BIF are at increased risk of developing SUD for psychoactive substances, such as alcohol, cannabis and other illicit drugs (Kepper, Monshouwer, van Dorsselaer, & Vollebergh, 2014; van Duijvenbode et al., 2015). Adolescents with an IQ score between 50 and 70 have a mild intellectual disability, which is a disability characterised by significant limitations in reasoning, learning, problem solving, and adaptive behaviour, impeding a range of everyday social and practical skills (American Psychiatric Association, 2013). Borderline intellectual functioning (IQ 71-85) is a condition that is used in health care when someone's limited intellectual functioning is the focus of clinical attention or has impact on treatment prognosis (American Psychiatric Association, 2013). The DSM-5 defines SUD as chronical, compulsive, and relapsing substance use (SU) behaviour in large amounts over a long time period, despite the expressed desire to stop and knowledge of adverse consequences (American Psychiatric Association, 2013). Numerous of such adverse psychological, medical, legal, and social consequences have been associated with SUD in adolescents with MID-BIF (Taggart, McLaughlin, Quinn, & Milligan, 2006). The estimated prevalence rate of SUD in the Netherlands is 5% of the MID-BIF population, which is higher than that of the general Dutch population (VanDerNagel et al., 2014). Therefore, there is an urgent need for SU(D) reducing intervention programmes adapted to the needs and cognitive abilities of adolescents with MID-BIF. Adapting interventions is crucial as neglecting intellectual and adaptive skills deficits leads to longer treatment duration and limited or even adverse treatment effects (Chen, Lawlor, Duggan, Hardy, & Eaton, 2006). Moreover, most existing interventions for SU(D) are based on a one-size-fits-all approach,

while research shows that individually tailored interventions (i.e., personalised) are more effective than untailored interventions (Conrod, Stewart, Comeau, & Maclean, 2006).

The current research examines two personalised intervention programmes developed to address problematic alcohol, cannabis, and other illicit drug use in adolescents with MID-BIF and behavioural problems. Intervention study 1 takes a nomothetic approach and intervention study 2 takes an idiographic perspective. In study 1, a quasi-experimental design with an intervention- and control group is used to generalise findings to the adolescent MID-BIF population by aggregating data across individuals from the intervention and control group. However, the pooled data from this nomothethic approach might not fit any specific individual, especially in a population of people with MID-BIF that has considerable heterogeneity in IQ and comorbid psychosocial problems. Therefore, study 2 employs an idiographic single case study design by focusing on the unique intervention effect and SUD development of the individual. The overall focus of both study 1 and study 2 is two-fold: assessing intervention effectiveness on decreasing SU and examining the relationship between changes in SU frequency and changes in other problematic behaviours and affect.

Comorbidity between SUD and other mental disorders is the rule rather than the exception for both disabled and non-disabled adolescents (van Duijvenbode et al., 2015). SUD can therefore be embedded within a broader domain of problems that reflect psychopathology. Studying *internalising* and *externalising* behaviours are two of such approaches that have often been pursued. Symptoms of depressive disorders, anxiety disorders, trauma and stress related disorders, and obsessive-compulsive disorders make up the internalising behaviours. Antisocial behaviours make up the externalising categorization, which entails—amongst others—symptoms of conduct disorder, antisocial personality disorder, and attention-deficit/hyperactivity disorder (Chan, Dennis, & Funk, 2008). In the population without a disability, regular use of alcohol, cannabis, or other illicit drugs has

frequently been associated with both externalising and externalising problems, such as aggression (e.g. Sacco, Bright, Jun, & Stapleton, 2015), delinquency (e.g. Monahan, Rhew, Hawkins, & Brown, 2014), depression (e.g. Davis, Uezato, Newell, & Frazier, 2008), and anxiety (e.g. Lai, Cleary, Sitharthan, & Hunt, 2015). Various underlying mechanisms may explain SUD comorbidity. One potential mechanism is inhibitory control, which has been found to account for the co-occurrence of alcohol use disorder and internalising disorders (Ellingson, Richmond-Rakerd, & Slutske, 2015). Although few studies have examined SUD comorbidity and underlying factors in the adolescent MID-BIF population, research does show that MID-BIF adolescents are three times more likely to develop persisting externalising and internalising problems compared to their non-disabled peers (Emerson, Einfield, & Stancliffe, 2011). However, broad psychopathology domains like externalising and internalising problems leave room for a wide range of individual differences (Hasin & Kilcoyne, 2012). The expression of SUD and comorbid problems in adolescents with MID-BIF thus also depends on more personal characteristics.

Extensive evidence documents that personality significantly correlates with externalising and internalising behaviours, cognitions, and affect (e.g. Hink et al., 2013). Personality can therefore be an important predictor for individual differences in SU behaviour and susceptibility for developing SUD (Krueger, Markon, Patrick, Benning, & Kramer, 2007). Woicik, Stewart, Phil, and Conrod (2009) distinguish four higher order personality profiles that are associated with a increased risk for problematic SU: anxiety sensitivity (AS), negative thinking (NT), impulsivity (IMP), and sensation seeking (SS). Each of these personality profiles has specific patterns and motives for SU. Negative thinkers, for example, can use alcohol or drugs through self-medication processes to cope with symptoms of depression, while impulsive substance users have deficits in behavioural inhibition which can cause SU (Woicik et al., 2009). AS and NT are relevant profiles for internalising problems, while IMP

and SS are representative of externalising forms of psychopathology (O'Leary-Barrett, Castellanos-Ryan, Pihl, & Conrod, 2016). Different patterns and motives for SU warrant personalised intervention programmes to effectively reduce SU, which is why SUD intervention programmes for adolescents without disabilities have used the four profiles to intervene at the level of personality risk (Conrod et al., 2006; Lammers et al., 2015). Adolescents with MID-BIF that fit one of the four profiles show increased alcohol and drug use, which makes these personality profiles valuable for identifying those at risk for developing SUD within this target group (Poelen, Schijven, Otten, & Didden, 2017). The two interventions examined in the present study differ in the programme's structure and therapeutic intensity (both interventions are explained in more detail in the methods section). Importantly, they both use cognitive behavioural therapy and motivational interviewing techniques to reduce SU in adolescents with MID-BIF by tailoring the intervention strategy to the participant's high-risk personality profile.

Due to the well-documented interrelatedness of SUD with both personality profiles and comorbid behavioural and affective problems, other interventions that target high-risk personality traits for SU reduce comorbid problems as well as SU (O'Leary-Barrett et al., 2016). Little is known, however, about the actual course of behavioural, cognitive, and affective changes before and during psychotherapy (Kazdin, 2009). Change processes in SU(D) intervention research are typically viewed as relatively smooth, as research often assesses the maintenance of intervention outcomes at intervals of several months (Hayes, Laurenceau, Feldman, Strauss, & Cardaciotto, 2007). The road to decreasing problematic SU, however, is anything but smooth. Instead, change processes of SU and related symptoms are discontinuous with shifts and fluctuations that become apparent when frequent (e.g. daily) measures are taken over a longer time span (Witkiewitz & Marlatt, 2007). An increasing body of research argues that SU(D) can be understood as a complex dynamic network of

behaviours and affective states that trigger each other, and in which seemingly minor discontinuous changes in particular behaviours or affective states can potentially set off a cascade of increased craving, SU, and other problematic behaviours (Kendler, Zachar, & Craver, 2011; Witkiewitz & Marlatt, 2007).

Well-established discontinuous change patterns in SU that emerge from interactions with other behaviours and affective states are sudden shifts towards a pattern of fewer SU (i.e. improvement) or more SU (i.e. relapse) (Hayes et al., 2007; Lutz et al., 2013). Principles from complex systems theory propose explanations for such sudden shifts (Gelo & Salvatore, 2016). In short, this theory states that certain general principles apply to change processes of various systems, ranging from physics to psychology (Thelen & Smith, 1994). One such principle, in terms of psychopathology, is that sudden discontinuous changes can be seen as phase transitions within a complex system of interacting behaviours, cognitions, emotions, and physiology (Gelo & Salvatore, 2016). A phase transition is a change of one stable behavioural, cognitive and affective pattern into a higher or lower stable pattern, that is characterised by a period of preceding *instability* (Scheffer et al., 2012). Importantly, both formal theory (Haken, 1983) and empirical findings (Scheffer et al., 2012) show that a period of instability gives rise to *critical fluctuations* (see Figure 1). This means that, on a timeline of repeated measurements of e.g. behaviour or affect, there is critical instability when the timeline fluctuates with a temporarily increased variability and unpredictability (Schiepek & Strunk, 2010). Hence, while a sudden reduction in SU frequency or sudden relapse may seem unexpected, complex systems theory states that identifiable critical fluctuations in related behaviours and affect can be an early warning signal for these sudden changes.

The current research examines two interventions that are designed to decrease alcohol, cannabis, and other illicit drug use in adolescents with MID-BIF. We hypothesise that 1) both studies will decrease SU as well as comorbid behavioural problems, that 2) changes in SU

depend on (complex) interactions with comorbid problems, and that 3) SU changes occur as phase transitions that are preceded by critical fluctuations in affect and behaviour. Specifically, for study 1 (quasi-experiment) it is expected that frequency and severity of SU, and externalising- and internalising behavioural problems show a stronger decrease in the intervention group compared to the control group. Moreover, it is expected that SU frequency and SU severity will only decrease stronger in the intervention condition when externalising- and internalising problems decrease stronger as well. In study 2 (single-case study with daily measurements) it is expected that in the intervention period, compared to baseline period, levels of positive affect will be higher, while negative affect, SU frequency and behavioural problems will be lower. Furthermore, it is expected SU behaviour is a complex dynamical system in which critical fluctuations of affect and problem behaviour precede sudden transitions in SU frequency (i.e. improvement or relapse).

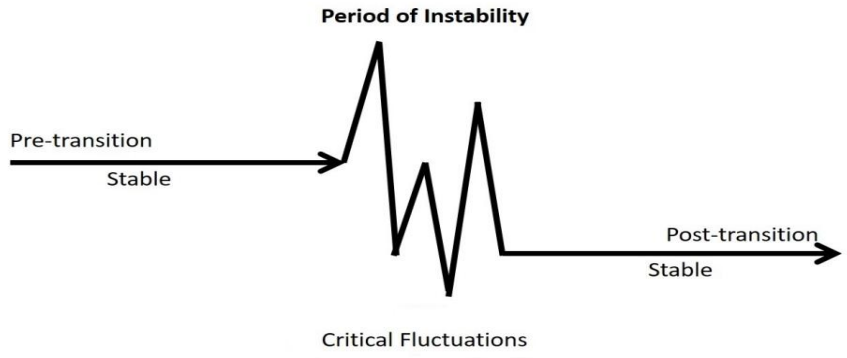

Figure 1. Conceptual illustration of a transition from one stable state to another stable state that is characterised by an instable period in which the system displays critical fluctuations.

Methods study 1*

Intervention study 1 had a quasi-experimental design with two arms and a 3-month follow-up. Adolescents with MID-BIF were screened at baseline, after which they were

* Methods and results from study 1 are described before methods and results from study 2.

assigned to either the intervention condition (*n*=34) or the control condition (*n*=32). Adolescents in the intervention condition attended the intervention programme ‘Take it Personal!’. Adolescents in the control condition received care as usual, which was neither standardised nor protocolled, and they were free to attend other programmes or therapies for their own specific problems. Within the intervention condition, eight groups of three or four adolescents were formed. Adolescents in each of these groups all had the same personality profile (NT, AS, IMP, SS) and were treated within the same treatment center. Data were collected between January 2015 and April 2017.

Participants

A total of 76 adolescents with MID-BIF were recruited in 11 treatment centers in the Netherlands that specialised in intra- and extramural care for people with MID-BIF and behavioural problems. Adolescents that met the following criteria were included: 1) between 14 and 30 years old, 2) total IQ ranging between 50 and 85, 3) use of alcohol, cannabis, and/or other illicit drugs was characterised by their clinician as anywhere between experimental SU and mild SUD according to the DSM-5 (American Psychiatric Association, 2013), and 4) having one of the four high risk personality profiles for SU (Woicik et al., 2013). There were 66 adolescents (47 males) from 11 treatment centers that met these criteria; they were assigned to either the intervention or control condition (see Figure 2).

Procedure

Treatment centers were informed of the intervention programme and invited to participate in this study. Adolescents that might be eligible to participate (i.e., meet inclusion criteria) were then approached by their personal caregiver or clinician who invited them to participate. Upon registration, adolescents were screened with self-reported questionnaires. The questionnaires included pictograms and images, and were administered via a web-application on a tablet computer that adolescents operated themselves. A researcher was

present that read every question out loud and, if necessary, provided further clarification with simple wording. An independent researcher used the Substance Use Risk Profile Scale (SURPS; Woicik et al., 2009) to determine high-risk personality profiles for SU per adolescent. An adolescent was identified as having a high-risk personality profile if the score on one of the four personality subscales (NT, AS, IMP, SS) was at least one standard deviation above the sample mean on that subscale. If more than one high-risk personality profile was identified in one adolescent, the independent researcher contacted that adolescent's personal clinician and appealed to his/her clinical experience to determine which profile explained the adolescent's SU the most. In such cases, their clinical judgment was the deciding factor.

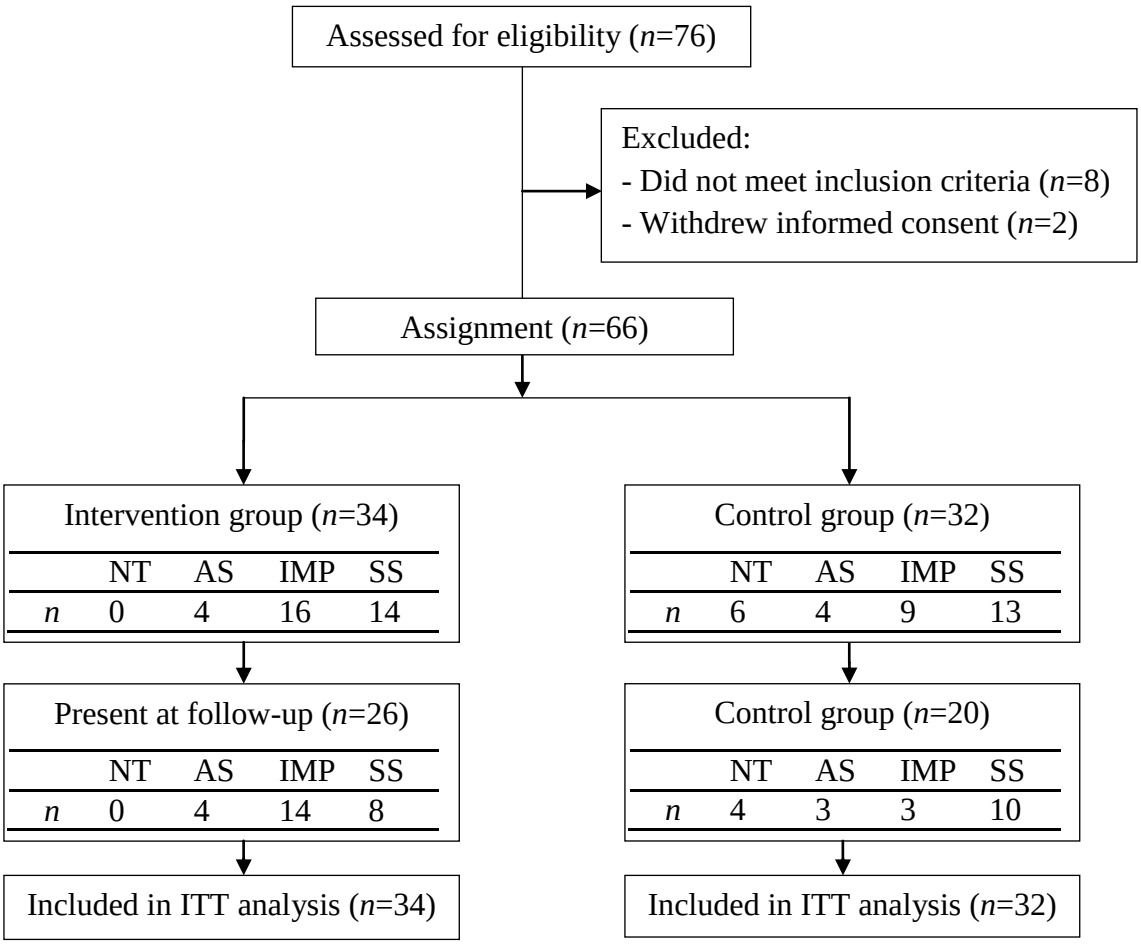

Figure 2. Flow diagram of enrolment and retention by treatment arm.

The assignment of adolescents to the intervention or control condition was conducted by the independent researcher based on a list that only included participant numbers, their corresponding treatment center and their personality profile. This assignment procedure could not fully be randomised because the intervention required group formation of three or four adolescents that had the same personality profile. Furthermore, it was decided to only form groups of adolescents that already received treatment in the same treatment center. This was done to lower the threshold for participation, as traveling between treatment centers on a weekly basis would cause too much inconvenience for adolescents and caregivers. Adolescents and parents (or legal representatives) were informed that the intervention was a programme to reduce alcohol and drug abuse, and that data would be processed anonymously. For each measurement, the adolescents received a € 5 gift card. Both adolescents and parents provided active informed consent. The Ethics Committee of Radboud University approved this study (ECSW2015-0903-303) and the trial was registered at the Dutch Trial Register (NTR5037; 15 April 2015).

Intervention

'Take it Personal!' was an intervention programme for adolescents and young adults (14-30 years old) with MID-BIF, behavioural problems and problematic SU. The intervention was based on the theory that someone's personality is a key construct for understanding SU (Conrod, 2006). For each of the four personality profiles (NT, AS, IMP, SS), different interventions were developed that were the same in structure but with their own personality-specific materials, games and (psychomotor) exercises. Each intervention comprised five 45-minute group sessions and five 30-minute individual sessions within a six week time span. Two qualified trainers (a clinical psychologist and a psychomotor therapist) conducted the group sessions together and for the individual sessions the adolescents were equally allocated to one of the two trainers. In each individual session, adolescents could bring a confidant from

their team of daily supervisors at their treatment center that they felt familiar with. This was done to maximise the transfer of training to daily life situations, and to ensure that adolescents felt safe and prepared for the group sessions. The intervention comprised three main components: 1) psycho-education, 2) behavioural coping skills, and 3) cognitive coping skills. The first phase focused on psycho-education regarding adolescent's personality profile and problematic behavioural expressions of that profile, such as SU or thrill seeking. Daily life experiences and coherent physical, cognitive and behavioural responses were analysed. In the coping skills components, adolescents learned to recognise and regulate personality-specific thoughts that caused problematic SU behaviour. Although the intervention could target any SU (alcohol, cannabis, hard drugs), adolescents set personalised goals and edited a personal 'changing plan' to deal with their own problematic behaviours and SU. Hence, in practice, the intervention addressed the use of whichever substance(s) that were most problematic for the individual. The content of 'Take it Personal!' is described in more detail in study protocol (Schijven, Engels, Kleinjan, & Poelen, 2015).

Measurements

For baseline screening the SURPS (Woicik et al., 2009) was used to distinguish the four high-risk personality profiles for SU. This 23-item questionnaire contained seven items that measure NT, six items for SS, five items for IMP and five items for AS. Each item could be scored on a 4-point Likert scale that ranged between (1) 'strongly agree' and (4) 'strongly disagree'. To adapt the SURPS to adolescents with MID-BIF, wording for some items was simplified and response options were complemented with pictograms of thumbs up and thumbs down. The SURPS has been shown to be valid in people with MID-BIF (Poelen et al., 2017). In the current sample, the SURPS demonstrated an acceptable internal consistency with Cronbach's $\alpha = 0.71$ for AS, 0.87 for NT, 0.62 for IMP and 0.67 for SS.

One item from the Substance Use and Misuse in Intellectual Disability Questionnaire (SumID-Q; VanDerNagel et al., 2011) was used to measure SU frequency. This item was asked for three substances separately. Adolescents thus answered the questions "How often do you drink alcohol / smoke weed / do hard-drugs?" with answer categories (1) 'never', (2) 'less than once a month', (3) 'every month', (4) 'every week', (5) 'almost every day'. To assess the severity of SU, the Alcohol Use Disorders Identification Test (AUDIT; Babor, Higgins-Biddle, Saunders, & Monteiro, 2001) and the Drug Use Disorders Identification Test (DUDIT; Berman, Bergman, Palmstierna, & Schlyter, 2003) were used, which are both incorporated in the SumID-Q. Each scale consisted of 10 items that could be rated on a five point Likert scale with answer categories ranging from (1) 'never' to (5) 'almost every day'. The AUDIT and DUDIT are complementary; their items relate to frequency and quantity of use, dependency and problems related to SU. An example is "How often couldn't you stop drinking/drug use?". Sum scores were calculated for AUDIT and DUDIT seperately. The AUDIT has been shown to be applicable in people with MID-BIF (van Duijvenbode, Didden, Korzilius, & Engels, 2017). In the current sample, both AUDIT and DUDIT showed good internal consistency with Cronbach's $\alpha = 0.75$ for the AUDIT and $\alpha = 0.81$ for the DUDIT.

Adolescent behavioural problems were measured with a Dutch version of the Youth Self Report (YSR; Achenbach, 1991; Verhulst, van der Ende, & Koot, 1997). The questionnaire included 118 items that could be rated on a 3-point Likert scale (0) not true at all, (1) somewhat or sometimes true, or (2) very true or often true. The YSR has three subscales: internalising problems, externalising problems, and total score. Externalising and internalising problems are subdivided into sets of items. Externalising problems consists of rule-breaking and aggressive behaviours in 33 items. Internalising problems has 31 items and measures anxious/depressed, withdrawn/depressed, and somatic complaints. Both externalising and

internalising show good internal consistency with Cronbach's $\alpha = 0.85$ for externalising and $\alpha = 0.88$ for internalising.

Analyses

Descriptive analyses were performed to examine baseline distributions of age, gender, total IQ, SU patterns and outcome measures between adolescents in the intervention and control group. Attrition analysis by means of logistic regression and Little's MCAR test indicated that values were missing completely at random, warranting the use of a multiple imputation strategy for intention-to-treat analyses, for which 100 datasets were drawn. All analyses were conducted in RStudio version 3.4.2 (RStudio Team, 2015).

Because the intervention addressed whichever substance or substances that was/were most problematic for each individual, each adolescent's most frequently used substance at baseline was compared with that substance at follow-up to examine intervention effectiveness. If more than one substance was equally frequently used at baseline, than that score was compared to the average score of these same substances at follow-up. For example, if a person used alcohol and cannabis daily at baseline and hard drugs monthly, than the baseline frequency or severity score for alcohol and cannabis (5: daily use) was compared to the average score of alcohol and cannabis at the follow-up measurement.

Four multilevel models were used to test the effect of the intervention on separate dependent variables: SU frequency, SU severity, externalising problems and internalising problems. In each of these four models, time, condition and the interaction time × condition were entered as fixed effects. In the models that assessed SU frequency and SU severity as dependent variables, it was also examined whether externalising and internalising problems moderated the intervention effect on SU. Therefore, in these two models assessing SU frequency and SU severity, the following three-way interactions were added alongside all

possible lower-order main effects and two-way interactions: time × condition × externalising behaviour problems and time × condition × internalising behaviour problems.

In all multilevel models, time was mean-centered, sum-to-zero contrasts were used, and random intercepts for time varying between participants and treatment centers were added to correct for data clustering. Externalising and internalising problems were only mean-centered in the two models assessing moderation effects. Statistical assumptions were checked, after multilevel models were performed with R package lme4 (Bates, Maechler, Bolker, & Walker, 2015). Goodness of model fit was assessed with conditional R^2 statistics obtained with R package MuMIn (Barton, 2018) which describe the proportion of variance explained by fixed and random effects (Nakagawa & Schielzeth, 2010) and by visually inspecting residual distributions and scatter plots of observed versus model fitted data points. To obtain *p* values, conditional *F* tests with Kenward-Roger approximation for degrees of freedom were performed on both models using R package afex (Singmann, Bolker, & Westfall, 2018).

Results study 1

Participant characteristics at baseline are displayed in Table 1. Only gender and the severity of alcohol use differed at baseline between intervention and control group. There were no significant differences at baseline between all other outcome variables and demographics. Overall, 24% of the adolescents were frequent alcohol users that reported weekly or daily alcohol consumption at baseline, 41% used cannabis weekly or daily, and 20% used hard drugs weekly or daily. In total, 23% of the adolescents were weekly or daily poly users of more than one substance.

Table 1.

Adolescent's baseline demographic and outcome characteristics.

Demographic / Score	Total sample (n = 66)	Intervention (n = 34)	Control (n = 32)	t /χ^2	p
Age	17.45 (2.76)	17.21 (2.67)	17.72 (2.88)	-0.75	.455
Total IQ	73.68 (7.92)	72.39 (9.13)	74.85 (6.91)	0.94	.329
Gender (male, %)	47 (71%)	20 (59%)	27 (84%)	3.20	.043*
Frequency alcohol use	2.71 (1.06)	2.92 (1.14)	2.50 (0.95)	1.59	.117
Frequency cannabis use	2.98 (1.52)	3.26 (1.52)	2.69 (1.49)	1.55	.125
Frequency hard drug use	1.97 (1.64)	2.17 (1.78)	1.75 (1.48)	1.05	.296
SU frequency [+]	3.58 (1.10)	3.82 (1.05)	3.31 (1.09)	2.16	.058
Alcohol use severity	8.12 (6.12)	10.02 (6.72)	6.09 (4.72)	2.74	.008*
Drug use severity	10.83 (9.44)	12.02 (10.33)	9.56 (8.35)	1.06	.292
SU severity [+]	13.32 (8.22)	15.24 (8.63)	11.28 (7.35)	2.13	.050
Externalising behaviour	17.21 (7.56)	18.44 (8.63)	15.91 (6.10)	1.37	.175
Internalising behaviour	9.35 (5.87)	9.29 (5.73)	9.41 (6.11)	0.77	.939

* Significant at $p < .05$. [+] Frequency and severity of each adolescent's most problematic substance (alcohol, cannabis or hard drugs). Except for gender, scores and demographics and outcome variable reflect *M* (*SD*).

Bivariate correlations were calculated between all outcome variables and are presented in Appendix 1 (whole sample) and Appendix 2 (separately for intervention and control group). Interestingly, externalising- and internalising problems at baseline and follow-up did not correlate with SU frequency and SU severity at neither baseline nor follow-up at $p < .05$.

The four models assessing SU frequency, SU severity, externalising- and internalising problems demonstrated acceptable goodness of fit with conditional R^2 = 0.53 for SU frequency, 0.68 for SU severity, 0.80 for externalising problems, and 0.84 for internalising problems. There were no residual outliers > 3 SD, and residuals were normally distributed.

Table 2 presents intervention effects on SU frequency and SU severity, estimated by the two-way interaction time × condition on SU frequency and SU severity, and all other included main and interaction effects involving externalising- and internalising problems. The intervention effects are visualised in Figure 3. SU frequency showed a stronger decrease in the intervention condition compared to the control condition, as the interaction time × condition was significant, $F(1, 62.78) = 8.24$, $p = 0.006$. Adolescents in the intervention condition did not show a stronger decrease in SU severity compared to the control condition, as the interaction time × condition was not significant, $F(1, 63.83) = 2.42$, $p = 0.125$. Moreover, as can be seen in Table 3, there was also no significant time × condition interaction on externalising problems, $F(1, 64.00) = 0.86$, $p = 0.306$, and internalising problems, $F(1, 64.00) = 0.19$, $p = 0.663$. This indicates that 'Take it Personal!' effectively reduced SU frequency, but not SU severity, externalising and internalising problems.

The moderating role of externalising- and internalising behavioural problems on SU was examined with the two-way interaction between time and behavioural problems on SU frequency and SU severity. Results indicate that the effect of time on SU frequency was not moderated by externalising problems, $F(1, 70.31) = 0.09$, $p = 0.764$. Internalising problems also did not moderate the effect of time on SU frequency, $F(1, 64.95) = 1.02$, $p = 0.316$. Furthermore, the effect of time of SU severity was not moderated by externalising problems, $F(1, 69.46) = 0.45$, $p = 0.507$, or internalising problems, $F(1, 63.93) = 0.18$, $p = 0.676$. This suggests that changes in SU frequency or SU severity did not depend on how problematic adolescents' externalising or internalising behaviours were. The last step of the analyses was

to examine the three-way interaction between behavioural problems, time, and condition, to determine if intervention effects on SU frequency and SU severity differ for adolescents depending on their externalising or internalising problems. Externalising problems did not moderate the interaction between time and condition on SU frequency, $F(1, 70.31) = 0.30$, $p = 0.588$, nor did internalising problems moderate this effect, $F(1, 64.95) = 0.01$, $p = 0.982$. Results indicate towards the same conclusion regarding SU severity; the interaction time × condition on SU severity was not moderated by externalising problems, $F(1, 69.46) = 0.51$, $p = 0.479$, and also internalising problems did not moderate this interaction, $F(1, 63.93) = 0.14$, $p = 0.709$.

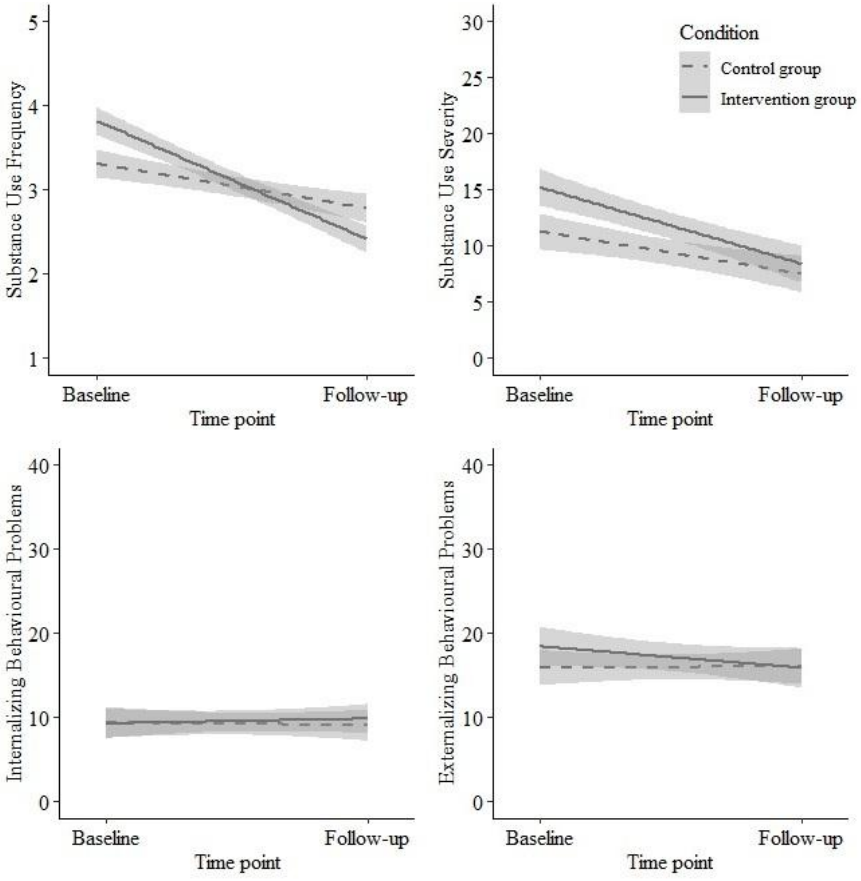

Figure 3. *Visualization of the significant intervention effect on SU frequency (top left), and the non-significant intervention effects on SU severity (top right), internalising- (bottom left) and externalising behavioural problems (bottom right).*

Table 2.

Fixed effects parameters of multilevel models predicting SU frequency and SU severity.

		SU frequency			SU severity		
	n df	dn df	*F*	*p*	dn df	*F*	*p*
Condition	1	61.02	0.12	.734	60.87	191.47	<.001***
Time	1	61.02	42.93	<.001***	63.83	40.97	<.001***
Externalising	1	86.70	0.40	.527	102.95	1.38	.243
Internalising	1	76.50	0.20	.660	89.02	0.01	.904
Time × Condition	1	64.95	8.24	.006***	63.83	2.42	.125
Time × Externalising	1	70.31	0.09	.764	69.46	0.45	.507
Time × Internalising	1	64.95	1.02	.317	63.93	0.18	.676
Condition × Externalising	1	86.70	1.45	.233	102.95	0.15	.703
Condition × Internalising	1	76.50	2.64	.108	89.02	0.94	.335
Time × Condition × Externalising	1	70.31	0.30	.588	69.46	0.51	.479
Time × Condition × Internalising	1	64.95	0.01	.981	63.93	0.14	.709

*** $p < .001$. n df = numerator degrees of freedom. dn df = denumerator degrees of freedom. Kenward-Roger approximation for degrees of freedom was used.

Table 3.

Fixed effects parameters of multilevel models predicting externalising- and internalising problems.

		Externalising behaviour			Internalising behaviour		
	n df	dn df	*F*	*p*	dn df	*F*	*p*
Condition	1	57.34	0.78	.380	54.95	0.11	.744
Time	1	64.00	0.86	.356	64.00	0.02	.894
Time × Condition	1	64.00	1.06	.306	64.00	0.19	.663

n df = numerator degrees of freedom. dn df = denumerator degrees of freedom. Kenward-Roger approximation for degrees of freedom was used.

Methods study 2

Intervention study 2 is a pilot study for an effectiveness study that uses a multiple baseline across-participants design, in which participants' baseline lengths are randomised. The pilot study presented here is a single-case study of the first participant to start and finish the intervention programme 'Take it Personal!+'. In this case-study, daily diary sampling was used during a randomly determined baseline phase of 12 days and the 11-week intervention programme, to model the change dynamics of one participant.

Participant

The participant (fictional name: Ben) was an 18-year-old male adolescent living in an assisted living facility for adolescents with MID-BIF and behavioural problems in the Netherlands. Ben had an acquired brain injury that resulted in a triple diagnosis: comorbid borderline intellectual functioning (IQ = 83), attention deficit hyperactivity disorder, and cannabis use disorder. On a daily basis he took medication to feel more relaxed and sleep better. He smoked cannabis daily, for which he had not received any treatment before starting 'Take it Personal!+'. The SURPS (Woicik et al., 2009) revealed that Ben scored the highest on personality profile 'anxiety sensitivity'.

Procedure

Clinicians from various living facilities for adolescents with MID-BIF in the Netherlands were informed of the intervention programme 'Take it Personal!+' and asked to invite any clients that might be eligible. As such, in consultation with a clinician, one of Ben's daily caregivers invited him to participate in order to try and reduce (i.e., preferably quit) his problematic cannabis use. An experienced therapist (who did not know Ben before) administered the SUMID-Q (VanDerNagel et al., 2011) and checked the DSM-5 criteria for SUD (American Psychiatric Association, 2013) to ensure that Ben was eligible to participate

in the intervention. The intervention study and programme were explained in word and writing, after which informed consent was obtained from both Ben and a legal representative.

Data collection in intervention study 2 comprised of daily diary measurements that were administered to Ben via a mobile phone application for ecological momentary research called 'Ethica' during a baseline phase (12 days) before the first therapy session and the entire intervention period (11 weeks). Every morning at 8 a.m., a survey consisting of questions about the previous day prompted on Ben's phone, after which he had until 3 p.m. to find a moment to reflect on the day before. On average, it took Ben less than two minutes to fill in one questionnaire after opening the app on his phone. Every three weeks, Ben received a €10 gift card for filling in the daily diary surveys.

Two days before the start of the baseline measurements, a researcher met with Ben and a confidant from his team of daily caregivers to personalise the items in the questionnaire and install Ethica. Personalisation of the items was done to the extent that it was verified if wording and answer categories matched Ben's language use (e.g., 'smoke weed', 'smoke pot' or 'blaze a joint'). Furthermore, the last item of the daily dairy questionnaire was to be determined by the participant himself. This was inspired by the systemic case formulation technique of Schiepek, Stöger-Schmidinger, Aichhorn, Schöller, and Aas (2016). This is an idiographic method in which therapist and client construct an individualised set of daily questions together, that captures the most important psychological and social variables for the client, who can then continuously receive his or her updated personal data profile in sessions throughout therapy. Ben could indicate which question he would like to ask himself in his daily diary that concerned a currently relevant problem in his daily life that could potentially be related to SU. Importantly, all items (except the personalised question) were extensively reviewed and tested by a panel of people with MID-BIF that develops and tests eHealth apps to guarantee user friendliness for the target group.

The intervention

'Take it Personal!+' was a personalised treatment programme that was designed for people of all ages with MID-BIF and mild to moderate SUD in psychoactive substances (alcohol, cannabis, hard drugs). The programme lasts 11 weeks with two 45-minute therapy sessions per week. Every week, one session is one-on-one between participant and therapist and in the other session a confidant person (from the participant's social network or team of daily caregivers) joins in to maximise generalisation to daily life situations and to ensure that the participant feels safe. The therapist uses cognitive behavioural therapy and motivational interviewing during a treatment that consists of the following key themes: behavioural change motivation (primary focus within first two weeks), setting goals and edit a personalised changing plan (continuously after week 2), psycho-education concerning personality profile to recognise signals of problematic behaviour (continuously after week 2), increasing self-agency (predominantly between week 3 and 7), behavioural and cognitive coping training (week 7 and 8), and relapse prevention (week 9, 10 and 11). A supporting mHealth application called 'TiP!' is used to strengthen generalization of learned skills to daily life. Via this app, participants can do exercises, receive personalised feedback, set personal goals, edit a changing plan, look up information on learned skills, and access mental support quickly with a help-button when they are in risky SU situations. Additionally, during the 11-week intervention period, the therapist has access to daily data on SU frequency (only item 10 of Table 1) which is discussed with the participant throughout the intervention. More detailed information about 'Take it Personal!+' can be found in the therapy manual (Gosens, VanDerNagel, Poelen, & de Jonge, 2019).

Measurements

Throughout the entire study period, a 13-item daily diary questionnaire was used (see Table 4) that Ben completed once per day via Ethica. The current study was the first to

construct and use such a daily diary questionnaire that was to be administered via a mobile phone application in people with MID-BIF. During questionnaire construction, it was important that items were 1) relevant to answer research questions, 2) expressed as variables that can fluctuate throughout time, 3) captured in the actual terms of the participant, and 4) generally well-adapted to the cognitive capacities of the MID-BIF target group.

Table 4.

The items from Ben's daily questionnaire.

1. Did you feel happy yesterday?
2. Did you feel fearful yesterday?
3. Did you feel confident yesterday?
4. Did you feel lonely yesterday?
5. Did you feel relaxed yesterday?
6. Did you feel sad yesterday?
7. Did you feel upset yesterday?
8. Were you bored yesterday?
9. Did you want to smoke weed yesterday?
10. How many joints did you smoke yesterday?
11. With who and where were you when you smoked weed yesterday?
12. Which other substances did you use yesterday besides weed?
13. Did you experience errors in your head yesterday?

Items 1 – 8 from Table 4 were derived from the Positive and Negative Affect Schedule (PANAS; Watson, Clark, & Tellegen, 1988). The PANAS is a questionnaire that originally contains 20 items, but as 20 items per day was considered too much, the most relevant items

were chosen for the purposes of this study. The other daily items measured craving (item number 9), context (11), SU (10 and 12), and a personalised item for problematic behaviour that was determined by the participant (13). All items for positive and negative affect, craving, and the personalised items were scored on a 5-point Likert scale ranging from (1) 'no, not at all' to (5) 'yes, very much'. In this study, item number 11 and 12 were used for descriptive purposes only, and answer categories for these items were determined in consultation with the participant and the confidant. The last personalised item was determined by Ben in consultation with the researcher and the confidant from his team of daily caregivers. Ben was asked which question he would like to ask himself in his daily diary that concerned a current problem that potentially could be SU-related in his daily life. Ben is oftentimes over-stimulated, which he calls 'having errors in my head'. For Ben, this is an unsettled feeling after experiencing more sensations than he can cope with. Ben feels like his cannabis use to some extend remedies this overstimulation.

Data analyses and visualization

In order to determine whether the intervention was effective in reducing SU frequency and comorbid problems, the mean scores during baseline and intervention phase were calculated for each of the continuous variables (item 1 – 10 and 13 from Table 1). A combination of visual inspection of the time series for SU frequency and statistical comparisons between the trends in baseline and intervention phases allowed for inferences about intervention effectiveness (Kazdin, 2009). For statistical comparisons between trends, Tau-U was calculated with R package effectsizescr (Giammusso, 2018). Tau-U is an effect size for single-case research that examines the proportion of non-overlap of data between two phases, while controlling for baseline trends (Parker, Vannest, Davis, & Sauber, 2011). Any missing values were imputed using Kalman filtering equations (Chen & Liu, 2000) with R package imputeTS (Moritz & Bartz-Beielstein, 2017).

Phase transitions were initially classified by visually inspecting the time series of SU frequency (Kazdin, 2009) to identify sudden shifts towards lower or higher levels of SU frequency (i.e., improvement or relapse). Quantitative decision rules for classifying sudden shifts were used to reassert any visually detected phase transitions in the time series of SU frequency. Based on Tang and DeRubeis' (1999) operationalisation of sudden shifts in psychotherapy, suddenly improving or relapsing SU had to involve a change that was at least 25% between the averages of two seven day periods. The criterion of 25% is relatively conservative (Kelly, Roberts, Ciesla, 2005; Lutz et al., 2013), thus ensuring that only considerably large mean shifts in SU frequency are used to identify phase transitions.

In order to analyse the changing complexity of comorbid problems and detect early warning signals, the 'dynamic complexity' measure was calculated using a moving window analysis. Dynamic complexity is designed for identifying critical fluctuations in short and coarse-grained time series (Schiepek & Strunk, 2010). It is comprised of a multiplication of measures for 1) variance in the time-series, 2) the time-series' fluctuation frequency and strength, and 3) the unpredictability of the distribution of values on a time-series. This measure is repeatedly calculated for each of the continuous items except SU frequency, in a moving window of freely selectable width (seven days in this study). This window shifts gradually along the time series without changing in width, such that first dynamic complexity is calculated for each item between day 1 and day 7, then between day 2 and day 8, and so on. This moving window technique allows for assessment of temporal stability of complexity over the course of a time-series (Pelletier-Baldelli, Andrews-Hanna, & Mittal, 2018). The 7-day window size was assumed appropriate as it controls for weekend effects and was expected to be short enough for predicting sudden mean shifts that indicate improvement or relapse.

The average dynamic complexity of all continuous items except SU frequency (i.e., item 1 until 9 and item 13 from Table 1) was then calculated for each 7-day time window. This can then be plotted on a time series to visualise change processes in average complexity of the 10 predicting items. The hypothesis that a sudden improvement or sudden relapse is preceded by critical fluctuations, operationalised here as increased dynamic complexity, was tested by plotting the time series of SU frequency and the time series of dynamic complexity in one graph on a standardised scale and visually assessing if a sudden jump is preceded by a peak in average dynamic complexity.

To gain more insight into the day-by-day processes before, during, and after a critical transition, the network structures (reflecting spatial correlations) of Ben's daily diary items measuring SU frequency, affect, craving, and over-stimulation (error in the head) were mapped using R package qgraph (Epskamp et al., 2012). Such network models use vector autoregression to capture linear interplays among multiple time series, i.e., how variability in each item's time series is influenced by contemporaneous (occurring on the same day) or lagged (occurring on the previous day) variability of each of the other items (Wright et al., 2015). Significant contemporaneous and lag-1 autocorrelations, and their strength (reflected in a β coefficient), were depicted in static images that show interrelatedness between items during the entire measurements period. Furthermore, the continuous changes in dynamic relations between these items were visualised in a movie that tracks the evolution of the network over time.

Results study 2

Ben completed 54 daily diary surveys in 75 days. For eight days, between day 52 and day 60, he did not fill in any diary surveys. As such, these days were omitted from analyses. The remaining 67-day period was used for analyses in which 54 diaries were completed (81%). Missing values were imputed via Kalman filtering (Chen & Liu, 2000). Mean scores and

standard deviations of 11 items measuring SU and comorbid problems were calculated for the baseline and intervention phase separately (see Table 5). Tau-U effect sizes (Parker et al., 2011) were computed to compare the overlap between baseline and intervention phase. Only SU was significantly lower in the intervention phase compared to the baseline phase (Tau-U = -0.47, $p = 0.017$), indicating a moderate effect. Ben was significantly more upset in the intervention phase compared to baseline (Tau-U = 0.58, $p = 0.005$).

Table 5.

Ben's descriptive statistics of baseline and intervention phase and Tau-U statistic of the difference between trends in the two phases.

	Baseline phase (*M, SD)*	Intervention phase (*M, SD)*	Tau-U
Happy	3.17 (0.58)	3.15 (0.53)	0.07
Scared	2.63 (0.64)	2.94 (0.61)	0.17
Confident	3.08 (0.52)	3.02 (0.64)	-0.16
Lonely	3.51 (0.99)	3.39 (0.64)	-0.37
Relaxed	2.75 (0.45)	2.89 (0.57)	0.16
Sad	3.09 (0.69)	3.16 (0.56)	0.06
Upset	2.33 (0.89)	3.26 (0.56)	0.58**
Bored	3.43 (0.66)	3.51 (0.66)	0.09
Craving	3.65 (0.98)	3.59 (0.71)	-0.05
Error	2.92 (0.52)	3.13 (0.86)	0.24
Substance use	2.51 (0.82)	1.53 (0.58)	-0.47*

* $p < .05$. ** $p < .01$. Except for substance use, all items were measured on a scale from (1) 'not at all' until (5) 'very much'.

In Figure 4A, the time series of Ben's daily number of smoked joints is visualised, which shows that between day 31 and 32, Ben's pattern of SU suddenly decreased. This sudden improvement was characterised as a phase transition, as before this sudden mean-shift, the mean number of smoked joints per day fluctuated in a relatively stable fashion around approximately 2.5 joints per day. After day 31, he attempted continuous abstinence. However, his SU then spiked on certain days (e.g., five joints on day 38). After his SU spiked again at day 49, he had to admit to himself that he could not stop using. This confronting moment marked the start of a relapse phase, in which he did not fill in any diaries between day 52 and day 60. Towards the end of the treatment he settled on a daily frequency of approximately two joints per day.

The time series of the 10 items for comorbid problems could be plotted and stacked on top of each other on separate lines. However, such a plot would make a synoptic overview of all of Ben's items difficult. Instead, the raw data resonance of Ben's scores on different outcome variables is presented in a tile plot that visualises all items in a single diagram (Figure 4B). Each row represents one item, while each column is a single day. The manifestation of the daily items is expressed by a colour-coded scale; each cell represents Ben's response on that respective day on a scale ranging from low scores (blue) via medium scores (yellow) to high scores (red). For example, on day 1 Ben reported that he was not at all upset but he experienced high craving.

Not included in the resonance diagram in Figure 4B are the two nominal variables (item 11 and 12 from Table 4), in which Ben reported daily where and with whom he used cannabis, and if he had used any other substances (alcohol or other drugs) besides cannabis. Interestingly, Ben never used cannabis together with other people; only when he was alone at home or outdoors (e.g., on the street). Furthermore, he never reported using any other substances besides cannabis.

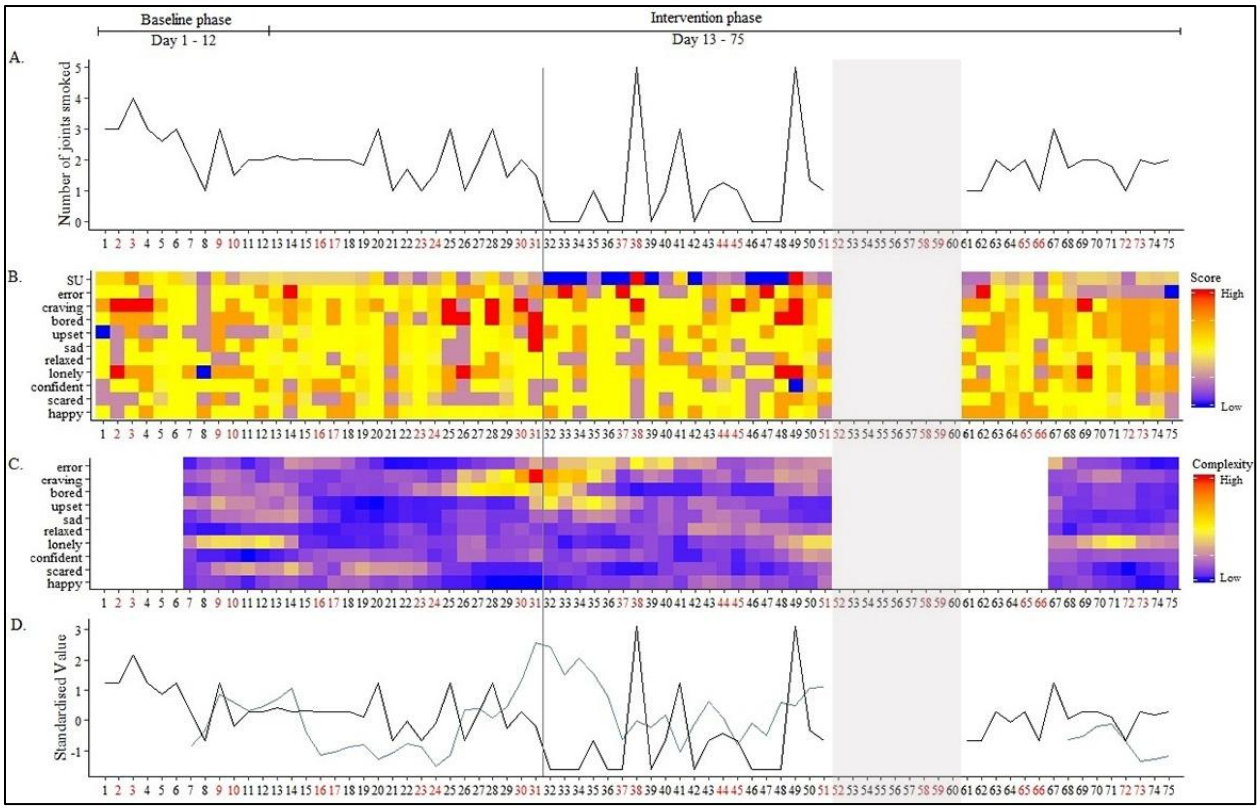

Figure 4. Combined graph reflecting Ben's raw data and complexity computations. Graph A is the time series of Ben's number of joints smoked per day. Graph B is a raw data resonance diagram which reflects, on a colour-coded scale, how high SU and comorbid problems were. Graph C uses the same colour-coded scale to visualise the complexity of each comorbid problem separately in a 7-day backwards window. Each tile indicates how high dynamic complexity in a particular item's time series was in the past seven days. For example, the tiles at index 7 represent dynamic complexity between day 1 and day 7, while tiles at index 75 reflect dynamic complexity between day 69 and day 75. Graph D is a plot of two time series on a standardised scale; the mean dynamic complexity of all comorbid problems (in a backwards 7-day window) in blue and SU frequency in black. The vertical gray line after day 31 and the gray bar after day 52 represent phase transitions. X-axes represent the days with weekend days (Saturday, Sunday) marked in red.

Dynamic complexity was calculated in a 7-day backwards window, which was visualised in a dynamic complexity resonance diagram in Figure 4C. Each cell represents the dynamic complexity of the previous 7 days of one item, and is colour-scaled relative to complexity in all other windows to visualise the strength of each item's complexity per window. What stands out in Figure 4C is the increased complexity prior to the sudden decrease in SU after day 31. The most erratic fluctuations can be seen in craving. The red tile in craving at index 31, for example, represents a 7-day backwards window, and thus visualises high complexity of fluctuations in craving between day 24 and day 31. A similarly increased complexity that precedes and accompanies the sudden decrease in SU can be seen in boredom and feeling upset. After the transition to a pattern of fewer SU, 'errors in the head' show an increased complexity.

The time series of the averaged dynamic complexity of all items in Figure 4C is visualised in blue in Figure 4D. A clear peak in average complexity (which should be read as reflecting a 7-day backwards window) can be seen preceding and accompanying the suddenly decreased pattern in SU frequency after day 31. This means that critical fluctuations acted as an early warning signal for the transition towards a lower, but unstable, pattern of SU. Interestingly, the mean dynamic complexity rises again leading up to relapse period, indicating an increasing instability in Ben's affective and behavioural system right before he had to admit that his abstinence attempt was unsuccessful.

In order to better understand the interrelatedness of affective states, behaviours, and SU, network structures that reflect contemporaneous and lag-1 relations between the daily diary items are visualised. Figure 5 presents network structures that only show significant associations ($p < .05$) and their strength (reflected in β coefficients). The positive association between SU and craving in Ben's contemporaneous network structure indicates that on days when he experiences high craving, he also smoked more cannabis on that day. Craving is also

positively associated with confidence and negatively associated with happiness, indicating that, on average, Ben experienced high craving on days when he reported high confidence and low happiness. The time-lagged associates provide insight into which affective states predict SU the next day. For example, the negative time-lagged association between feeling upset and SU indicates that Ben smoked fewer joints after a day in which he felt more upset and vice versa. Furthermore, SU is related to Ben's confidence, as high SU leads to more confidence the next day, which, in turn, leads to more confidence and more SU the day after.

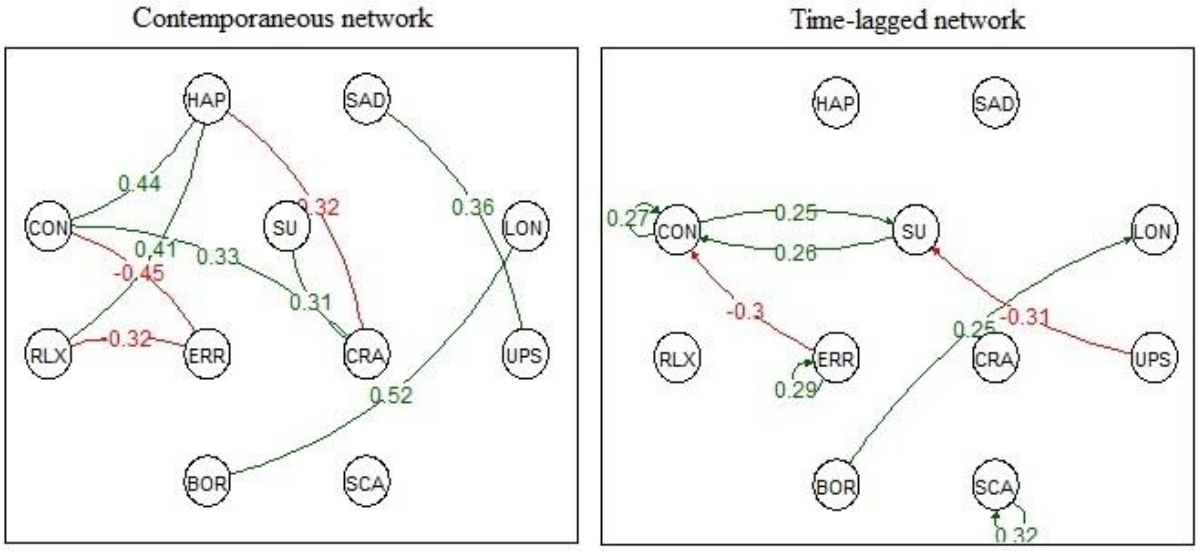

Figure 5. Contemporaneous and time-lagged (lag-1) network structures during the entire 75-day measurement period. Green lines are significant positive associations. Red lines are significant negative associations. HAP = happy; SAD = sadness; CON = self-confidence; SU = substance use; LON = loneliness; ; RLX = relaxed; ERR = error in the head; CRA = craving; UPS = upset; BOR = bored ; SCA = scared.

The interrelatedness over the entire 75-day time span (with exception of relapse period between day 52 – 60) is reflected in Figure 5. However, as was illustrated in Figure 4, scores on affect and SU behaviour change on a day-to-day basis and continuously fluctuate

throughout the 75-day period. Day-to-day changes and fluctuations throughout time also cause changes in the contemporaneous and time-lagged interrelations between affect and (SU) behaviour. For example, Figure 5 demonstrates that on average during the 2.5 month period, Ben's SU only had time-lagged associations with feeling upset and self-confidence. However, this does not mean that SU was only associated with these affective states. When zooming in on smaller chunks of the time-series, for example by assessing windows of two weeks (instead of the whole 2.5 months) and tracking its evolution over time, the dynamic and shifting nature of a network model becomes visible. The complexity of these continuous changes in Ben's behavioural and affective network is visualised in a movie (see https://www.dropbox.com/s/tdlp8rx4xvrutmm/Movie_SUD_MID_BIF_majorthesis_DH.avi?dl=0). This video visualises the dynamic nature of SUD until Ben's relapse period after day 51. At the start of the baseline phase, Ben's craving was predicted by the SU (pink circle) of the previous day, but later during the intervention 'errors in the head' and upset feelings show the strongest time-lagged associations with his craving for SU. This means that, contrary to what his static network visualisation (Figure 5) suggests, Ben's craving is not only associated with SU frequency, upset feelings, and confidence throughout the 75-day time period. Instead, the development of Ben's SUD can be characterised as a complex dynamical system in which day-to-day associations between different affective states and behaviours influence each other, craving and SU frequency differently over time.

Discussion

In this study we examined two interventions that were designed to decrease alcohol, cannabis, and other illicit drug use in adolescents with MID-BIF, using a nomothetic design (quasi experimental; intervention study 1) and an idiographic design (case study; intervention study 2). We expected that 1) both interventions would decrease SU as well as comorbid behavioural and affective problems, 2) SU would depend on (complex) interactions with

changes in comorbid problems, and 3) SU changes would occur as phase transitions that were preceded by critical fluctuations in affect and behaviour. For both interventions we found decreases in SU frequency, but not in comorbid problems. The first hypothesis could therefore only partly be confirmed. In intervention study 1, we found that adolescents' SU frequency decreased stronger in the intervention group compared to the control group, whereas there were no changes between the two groups on SU severity, externalising and internalising problems. For intervention study 2 we found that, compared to baseline phase, Ben only showed decreases in SU frequency during the intervention phase, whereas related behavioural and affective problems did not decrease. We did not find moderating interaction effects for externalising and internalising problems on changes in SU frequency or severity over time, indicating that the second hypothesis could not be confirmed in study 1. The results of study 2, however, confirmed our second and third hypothesis. We demonstrated that SUD can be characterised as a complex dynamic system in which SU continuously interacts with affect and behaviour. Moreover, by using the complexity of day-to-day fluctuations in time-series analyses, we were able to show that sudden shifts in Ben's SU frequency (improvement or relapse) reflect phase transitions that were preceded by critical fluctuations in affect and behaviour.

In intervention study 1, adolescents' changes in SU and related problems were assessed at the group level with a design that examines externalising and internalising problems. We found significant decreases in SU, which is in line with other studies demonstrating the effectiveness of personality-tailored intervention approaches in alcohol using adolescents without MID-BIF (Conrod et al., 2006; Lammers et al., 2015). Importantly, this extends existing literature on personality-tailored interventions for SU in two ways. First, this approach, when adapted to the cognitive abilities of the target group, reduces SU in adolescents with MID-BIF. Second, the use of a broader range of substances can effectively

be reduced, i.e., alcohol, cannabis and other illicit drug use. ‘Take it Personal!’ thus seems to meet the needs of this vulnerable high-risk target group, and contributes to the relatively small evidence base of existing effective SU(D) interventions for adolescents with MID-BIF (van Duijvenbode et al., 2015). The design of study 1, however, did not lend itself to expose any changes in related externalising and internalising problems, or interactions thereof with SU, at the group level. It is possible that the domains of externalising and internalising problems were too broad to show changes at the group-level between two time points.

Study 2 sought to explore an adolescent’s change processes before and during the ‘Take it Personal!+’ intervention. In depth knowledge of *how* individual changes occur is necessary for further development and personalisation of intervention programmes (Hekler et al., 2016). Although there were no overall improvements in time series trends for Ben’s affect, craving, or related behaviours in the intervention phase compared to the baseline phase, time series analyses showed that Ben’s SU, craving, affect, and related behaviours fluctuated from day to day while continuously interacting with each other. That is, there was no overall improvement over the entire 75-day measurement period, but zooming in on shorter time spans within the 75-day time series and tracking the evolution of Ben’s network, revealed that the connectivity between different affective states and SU behaviour changed over time. SUD can therefore be understood as an complex interplay between continuously interacting affective states and (SU) behaviours that is unique for each individual. In Ben’s case, some weeks upset feelings triggered his SU, while in other weeks it seemed to depend the most on cognitive over-stimulations.

Dynamic network visualisations allow for examining person-specific mechanisms which can have important clinical implications as they may provide knowledge that can aid future intervention development and, importantly, can be used directly in clinical MID-BIF practice. Therapists could use such knowledge to identify network connections between specific

behaviours or affective states that cause or maintain unfavourable SU patterns. This may be particularly helpful for adolescents with MID-BIF who, due to their intellectual deficits, often experience difficulties in recognising and expressing their own behavioural and affective mechanisms in relation to their SU. The networks can thus provide therapists with directions for further tailoring their therapeutic approach to those connections that need alteration for a particular individual in order to maximise probability of improvement. In Ben's case, he had a period when his network model indicated positive associations between craving and cognitive over-stimulations ("errors in the head"). This information might have made Ben's therapist shift therapeutic focus in sessions to these over-stimulations by e.g. exposing Ben to mindfulness exercises to cope with these sensory overloads. It therefore follows that individual-specific mechanistic knowledge can be used, in addition to group-level knowledge, for the development of future interventions by identifying person-specific clusters of symptoms related to SU that can be targeted with intervention materials and exercises.

Within this complex network of interacting affect and behaviours, principles of complex systems theory can be tested (Hayes et al., 2007). Changes in Ben's affect and behaviour did not happen gradually over time. Instead, phase transitions could be detected on the time series of Ben's SU frequency, with peaking dynamic complexity preceding transitions towards improving or relapsing SU. This is the first study to show that identifiable fluctuations in an MID-BIF adolescent's behaviour and emotion can be an early warning signal for phase transitions, thereby further bolstering a growing body of research on early warning signals in psychotherapy. The meaning and clinical implications hereof should be interpreted within the broader context of complex systems theory. It must be emphasised that critical fluctuations are not predictors of specific kinds of phase transitions, but rather general indicators of instability that are potentially predictive because they often result in a phase transition in the near future (Gelo & Salvatore, 2016). Other clinical (single-case) studies show that critical

fluctuations can precede very different phase transitions towards healthier and unhealthier states in different psychopathologies (Scheffer et al., 2012). Instability signals a period in which the system has an increased sensitivity to external influences (Thelen & Smith, 1994). Therefore, clinical interventions may have their greatest impact if they are targeted at these sensitive periods (Granic, 2005). In Ben's case, this might mean that therapy sessions during an instable period (e.g. day 24 – 31, Figure 4D) had increased potential to realise sudden improvements compared to sessions during more stable periods. Further clinical (MID-BIF) research on this hypothesis, using large samples, is warranted. If confirmed, it might enable therapists to timely adapt therapeutic efforts to such instable periods.

The main strength of this research is that it provides group- and individual-level evidence of intervention effectiveness and change processes. Intervention study 2 was a pilot study with daily diary measurements that were taken across the baseline and the entire intervention period, thereby evaluating network models and critical fluctuations with an appropriate timeline (Kazdin, 2009). This also illustrates the feasibility of daily dairy sampling in adolescents with MID-BIF practice. Nevertheless, future research on SUD change processes in adolescents with MID-BIF should note that this intense data collection method is challenging for participants. Ben had a high intrinsic motivation to achieve his personal intervention goals, which, in combination with his caregivers' abiding support, resulted in filling in 81% of his daily diary surveys before and after the relapse period. However, Ben experienced a relapse period in which he did not fill in any diary surveys for eight days. High compliance rates are pivotal for interpreting results, especially after a phase transition towards relapsing SU. Future research could therefore explore the possibilities of finding potentially predictive early warning signals in passively collected data, such as contextual, movement, skin conductance or heart rate data.

This research has several limitations. First, study 1 was quasi-experimental as the standards for a randomised controlled could not be met. Attribution to intervention or control condition could not fully be randomised and the total sample size was small, which likely caused a relative underrepresentation of internalising personality profiles in our sample. Second, both study 1 and 2 do not assess any long-term intervention effects on SU and related problems. Third, because study 2 was the first to employ the daily diary method in adolescents with MID-BIF, reliability and validity of the data collection method has not yet been documented for this target group. However, daily diary sampling has been employed in SUD research in non-disabled people (Serre, Fatseas, Debrabant, Alexandre, Auriacombe, & Swendsen, 2012) and has proven to be valid and reliable for assessing a range of behaviours and affect in difficult clinical populations (e.g. psychotic patients; Kuepper, Oorschot, Myin-Germeys, Smits, van Os, & Henquet, 2013). An important first step for future research is to validate the sampling method for this population. The last limitation is that study 1 and 2 only allow for quantitative inferences about change processes. However, changing interactions, instability and critical phase transitions are ultimately qualitative in nature. What changed for Ben during e.g. the apparent quantitative substance using phase transitions? Mixed methods daily diary items will lead to a better understanding of the change processes that adolescents with SUD and MID-BIF experience. The qualitative component can be implemented in the mobile phone application by adding an open box in the daily diary app that invites the participant to describe daily experiences or by qualitative analyses of session reports written by the therapist.

People who successfully overcame SUD describe the road towards recovery from SU problems as a long and oftentimes confronting road of self-discovery (Mackintosh & Knight, 2012). Understanding your personal mechanisms in relation to SU is a fundamental task for changing your SU, and this requires deep self-reflections. The intellectual limitations of

adolescents with MID-BIF form a barrier for thorough self-reflections, making the difficult challenge overcoming SU related problems even more troublesome. This study demonstrated that the personalised approach of interventions targeting high risk personality traits for SU is effective in decreasing SU, and visualised how individual change occurs during the intervention. The daily diary outcomes do not only hold important scientific potential for better understanding change processes in recovering from SU problems, clinical MID-BIF practice could potentially integrate such personal data in the intervention for further personalisation of care. If such data, for example as network visualisations, are fed back to therapists throughout the intervention, they can provide therapists with deeper knowledge on the participant's SU related behavioural and affective patterns. In turn, this would enable therapists to further tailor their approach to the needs of the individual, so that adolescents like Ben, their environments, and society might all reap the benefits.

References

Achenbach, T. M. (1991). *Manual for the Youth Self-Report and 1991 profile.* Burlington, VT: University of Vermont, Department of Psychiatry.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, DC: American Psychiatric Association.

Babor, T. F., Higgins-Biddle, J. C., Saunders, J. B., & Monteiro, M. G. (2001). *AUDIT. The alcohol use disorders identification test. Guidelines for use in primary care.* Geneva: World Health Organisation.

Barton, K. (2018). MuMIn: Multi-model inference. R package version 1.42.1. Derived from: https://CRAN.R-project.org/package=MuMIn.

Bates, D., Maechler, M., Bolker, B., & Walker, S. (2015). Fitting Linear Mixed-Effects Models using lme4. *Journal of Statistical Software, 67,* 1-48.

Berman, A. H., Bergman, H., Palmstierna, T., & Schlyter, F. (2003). *DUDIT. The drug use identification test manual*. Stockholm: Karolinska Institutet, department of clinical neuroscience.

Carroll Chapman, S. L., & Wu, L. T. (2012). Substance abuse among individuals with intellectual disability. *Research in Developmental Disabilities, 33,* 1147-1156.

Chan, Y. F., Dennis, M. L., & Funk, R. R. (2008). Prevalence and comorbidity of major internalizing and externalizing problems among adolescents and adults presenting to substance abuse treatment. *Journal of Substance Abuse Treatment, 34,* 14-24.

Chen, C. Y., Lawlor, J. P., Duggan, A. K., Hardy, J. B., & Eaton, W. W. (2006). Mild cognitive impairment in early life and mental health problems in adulthood. *American Journal of Public Health, 96,* 1772-1778.

Chen, R., & Liu, J. S. (2000). Mixture kalman fiters. *Journal of the Royal Statistical Society Series-B Statistical Methodology, 62*, 493-508.

Conrod, P. J., Stewart, S. H., Comeau, N., & MacLean, A. M. (2006). Efficacy of cognitive-behavioral interventions targeting personality risk factors for youth alcohol misuse. *Journal of Clinical Child and Adolescent Psychology, 35,* 550-563.

Davis, L., Uezato, A., Newell, J. M., & Frazier, E. (2008). Major depression and comorbid substance use disorders. *Current Opinion in Psychiatry, 21,* 14-18.

Ellingson, J. M., Richmond-Rakerd, L. S., & Slutske, W. S. (2015). Brief report: cognitive control helps explain comorbidity between alcohol use disorder and externalizing disorders. *Journal of Studies on Alcohol and Drugs, 76,* 89-94.

Emerson, E., Einfield, S., & Stancliffe, R. J. (2011). Predictors of the persistence of conduct difficulties in children with cognitive delay. *Journal of Child Psychology and Psychiatry, 52,* 1184–1194.

Epskamp, S., Cramer, A. O. J., Waldorp, L. J., Schmittmann, V. D., & Borsboom, D. (2012). qgraph: Network visualizations of relationships in psychometric data. *Journal of Statistical Software, 48,* 1-18.

Gelo, O. C. G., & Salvatore, S. (2016). A dynamic systems approach to psychotherapy: A meta-theoretical framework for explaining psychotherapy change processes. *Journal of Counseling Psychology, 63,* 379-395.

Giammusso, I. (2018). effectsizescr: Indices for single-case research. R package version 0.1.0. Derived from: https://CRAN.R-project.org/package=effectsizescr.

Gosens, L., VanDerNagel, J., Poelen, E. A. P., & de Jonge, J. (2019). *Handleiding Take it Personal!+. Gepersonaliseerde behandeling voor cliënten met een lichte verstandelijke beperking en problematisch middelengebruik.* Nijmegen: Pluryn.

Granic, I. (2005). Timing is everything: Developmental psychopathology from a dynamic systems perspective. *Developmental Review, 25,* 386-407.

Haken, H. (1983). *Synergetics: an introduction. Non-equilibrium phase transition and self-selforganisation in physics, chemistry and biology.* Berlin: Springer Verlag.

Hasin, D., & Kilcoyne, B. (2012). Comorbidity of psychiatric and substance use disorders in the United States: current issues and findings from the NESARC. *Current Opinion in Psychiatry, 25,* 165-171.

Hayes, A. M., Laurenceau, J.-P., Feldman, G., Strauss, J. L., & Cardaciotto, L. (2007). Change is not always linear: The study of nonlinear and discontinuous patterns of change in psychotherapy. *Clinical Psychology Review, 27,* 715-723.

Hekler, E. B., Klasnja, P., Riley, W. T., Buman, M. P., Huberty, J., Rivera, D. E., & Martin, C. A. (2016). Agile science: creating useful products for behaviour change in the real world. *Translational Behavioral Medicine, 6,* 317-328.

Hink, L. K., Rhee, S. H., Corley, R. P., Cosgrove, V. E., Hewitt, J. K., Schultz-Heik, R. J., ... Waldman, I. D. (2013). Personality dimensions as common and broadband-specific features for internalizing and externalizing disorders. *Journal of Abnormal Child Psychology, 41,* 939-957.

Kazdin, A. E. (2009). Understanding how and why psychotherapy leads to change. *Psychotherapy Research, 19,* 418-428.

Kelly, M. A. R., Roberts, J. E., & Ciesla, J. A. (2005). Sudden gains in cognitive behavioral therapy for depression: when do they occur and do they matter? *Behaviour Research and Therapy, 43,* 703-714.

Kendler, K. S., Zachar, P., & Craver, C. (2011). Mental disorders and mechanistic property clusters reply. *Psychological Medicine, 41,* 1566-1566.

Kepper, A., Monshouwer, K., Van Dorsselaer, S., & Vollebergh, W. (2011). Substance use by adolescents in special education and residential youth care institutions. *European Child & Adolescent Psychiatry, 20,* 311–319.

Krueger, R. F., Markon, K. E., Patrick, C. J., Benning, S. D., & Kramer, M. D. (2007). Linking antisocial behavior, substance use, and personality: An integrative quantitative model of the adult externalizing spectrum. *Journal of Abnormal Psychology, 116,* 645-666.

Kuepper, R., Oorschot, M., Myin-Germeys, I., Smits, M., van Os, J., & Henquet, C. (2013). Is psychotic disorder associated with increased levels of craving for cannabis? An experience sampling study. *Acta Psychiatrica Scandinavica, 128,* 448-456.

Lai, H. M. X., Cleary, M., Sitharthan, T., & Hunt, G. E. (2015). Prevalence of co-morbid substance use, anxiety and mood disorders in epidemiological surveys, 1990-2014: A systematic review and meta-analysis. *Drug and Alcohol Dependence, 154,* 1-13.

Lammers, J., Goossens, F., Conrod, P., Engels, R., Wiers, R. W., & Kleinjan, M. (2015). Effectiveness of a selective intervention program targeting personality risk factors for alcohol misuse among young adolescents: results of a cluster randomized controlled trial. *Addiction, 110,* 1101-1109.

Lutz, W., Ehrlich, T., Rubel, J., Hallwachs, N., Röttger, M.-A., Jorasz, C., … Tschitsaz-Stucki, A. (2013). The ups and downs of psychotherapy: Sudden gains and sudden losses identified with session reports. *Psychotherapy Research, 23,* 14-24.

Mackintosh, V., & Knight, T. (2012). The notion of self in the journey back from addiction. *Qualitative Health Research, 22,* 1094-1101.

Monahan, K. C., Rhew, I. C., Hawkins, J. D., & Brown, E. C. (2014). Adolescent pathways to co-occuring problem behavior: The effects of peer delinquency and peer substance use. *Journal of Research on Adolescence, 24,* 630-645.

Moritz, S., & Bartz-Beielstein, T. (2017). imputeTS: Time series missing value imputation in R. *R Journal, 9, 207-218.*

Nakagawa, S., & Schielzeth, H. (2010). Repeatability for Gaussian and non-Gaussian data: a practical guide for biologists. *Biological Reviews, 85,* 1469-1485.

O'Leary-Barrett, M., Castellanos-Ryan, N., Pihl, R. O., & Conrod, P. J. (2016). Mechanisms of personality targeted intervention effects on adolescent alcohol misuse, internalizing and externalizing symptoms. *Journal of Consulting and Clinical Psychology, 84,* 438-452.

Parker, R. I., Vannest, K. J., Davis, J. L., & Sauber, S. B. (2011). Combining nonoverlap and trend for single-case research: Tau-U. *Behavior Therapy, 42,* 284-299.

Pelletier-Baldelli, A., Andrews-Hanna, J. R., & Mittal, V. A. (2018). Resting state connectivity dynamics in individuals at risk for psychosis. *Journal of Abnormal Psychology, 127,* 314-325.

Poelen, E. A. P., Schijven, E. P., Otten, R., & Didden, R. (2016). Personality dimensions and substance use in individuals with mild to borderline intellectual disabilities. *Research in Developmental Disabilities, 63,* 142-150.

RStudio Team. (2015). *RStudio: Integrated development for R.* Boston, MA: RStudio Inc.

Sacco, P., Bright, C. L., Jun, H. J., & Stapleton, L. M. (2015). Developmental relations between alcohol and aggressive behavior among adolescents: Neighborhood and sociodemographic correlates. *International Journal of Mental Health and Addiction, 13,* 603–617.

Scheffer, M., Carpenter, S. R., Lenton, T. M., Bascompte, J., Brock, W., Dakos, V., ... Vandermeer, J. (2012). Anticipating critical transitions. *Science, 338,* 344-348.

Schiepek, G., Stöger-Schmidinger, B., Aichhorn, W., Schöller, H., & Aas, B. (2016). Systemic cse formulation, individualized process monitoring, and state dynamics in case of dissociative identity disorder. *Frontiers in Psychology, 7¸* 1-11.

Schiepek, G., & Strunk, G. (2010). The identification of critical fluctuations and phase transitions in short term and course-grained time series – a method for real time monitoring of human change processes. *Biological Cybernetics, 102,* 197-207.

Schijven, E. P., Engels, R. C. M. E., Kleinjan, M., & Poelen, E. A. P. (2015). Evaluating a selective prevention program for substance use and comorbid behavioral problems in adolescents with mild to borderline intellectual disabilities: Study protocol of a randomized controlled trial. *BMC Psychiatry, 15,* 1-7.

Singmann, H., Bolker, B., Westfall, J., & Aust, F. (2018). afex: Analysis of Factorial Experiments. R package version. 0.19-1. Derived from: https://CRAN.R-project.org/package=afex.

Taggart, L., McLaughlin, D., Quinn, B., & Milligan, V. (2006). An exploration of substance misuse in people with intellectual disabilities. *Journal of Intellectual Disability Research, 50,* 588-597.

Tang, T. Z., & DeRubeis, R. J. (1999). Sudden gains and critical sessions in cognitive-behavioral therapy for depression. *Journal of Consulting and Clinical Psychology, 67,* 894-904.

Thelen, E., & Smith, L. B. (1994). *A dynamic systems approach to the development of cognition and action.* Cambridge, MA: The MIT Press.

Van Duijvenbode, N., Didden, R., Korzilius, H. P. L. M., & Engels, R. C. M. E. (2017). Attention bias in problematic drinkers with and without mild to borderline intellectual disability. *Journal of Intellectual Disability Research, 61,* 255-265.

Van Duijvenbode, N., VanDerNagel, J. E. L., Didden, R., Engels, R. C. M. E., Buitelaar, J. K., Kiewik, M., & de Jong, C. A. J. (2015). Substance use disorders in individuals with mild to borderline intellectual disability: Current status and future directions. *Research in Developmental Disabilities, 38,* 319-328.

VanDerNagel, J. E. L., Kiewik, M., Postel, M. G., van Dijk, M., Didden, R., Buitelaar, J. K., & de Jong, C. A. J. (2014). Capture recapture estimation of prevalence of mild intellectual disability and substance use disorder. *Research in Developmental Disabilities, 35,* 808-813.

Verhulst, F. C., van der Ende, J., & Koot, H. M. (1997). *Handleiding voor de Youth Self-Report (YSR).* Rotterdam: Sophia Kinderziekenhuis, afdeling kinder- en jeugdpsychiatrie.

Watson, D., Clark. L. A., & Tellengen, A. (1988). Development and validation of brief measures of positive and negative affect – the PANAS scales. *Journal of Personality and Social Psychology, 54,* 1063-1070.

Witkiewitz, K., & Marlatt, G. A. (2007). Modeling the complexity of post-treatment drinking: It's a rocky road to relapse. *Clinical Psychological Review, 27,* 724-738.

Woicik, P. A., Stewart, S. H., Phil, R. O., & Conrod, P. J. (2009). The substance use risk profile scale: a scale measuring traits linked to reinforcement-specific substance use profiles. *Addictive Behaviors, 34,* 1042-1055.

Wright, A. G. C., Beltz, A. M., Gates, K. M., Molenaar, P. C. M., & Simms, L. J. (2015). Examining the dynamic structure of daily internalizing and externalizing behaviour at multiple levels of analysis. *Frontiers in Psychology, 6,* 1-20.

Appendix 1. *Bivariate correlations of study 1 outcome measures.*

	1.	*2.*	*3.*	*4.*	*5.*	*6.*	*7.*	*8.*	*9.*	*10.*	*11.*	*12.*	*13.*	*14.*	*15.*	*16.*	*17.*	*18.*
1. B alc	1																	
2. FU alc	.13	1																
3. B can	.10	-.12	1															
4. FU can	.07	-.05	.56**	1														
5. B drug	.11	-.11	.57**	.19	1													
6. FU drug	-.19	-.20	.36*	.59**	.31*	1												
7. B freq	.41**	.00	.80**	.43**	.52**	.33**	1											
8. FU freq	-.01	.35*	.22	.64**	-.02	.46**	.30*	1										
9. B AUD	.53**	.14	.16	.07	.15	-.04	.34**	-.02	1									
10. FU AUD	.07	.53**	.07	.01	.07	-.11	.08	.15	.63**	1								
11. B DUD	.18	-.04	.57**	.25*	.69**	.27*	.56**	.04	.26*	.18	1							
12. FU DUD	.16	-.19	.57**	.61**	.42**	.72**	.51**	.40**	.30*	.14	.66**	1						
13. B sev	.36*	.00	.55**	.21	.66**	.20	.63**	.02	.48**	.36*	.92**	.63**	1					
14. FU sev	.18	-.12	.38**	.44**	.46**	.52**	.40**	.38**	.33*	.37*	.57**	.85**	.65**	1				
15. B EPB	-.02	.30*	.10	.14	.01	-.12	.06	.17	.11	.33*	.19	.05	.19	.11	1			
16. FU EPB	-.17	.13	.02	.13	-.05	-.11	-.07	.15	-.06	.23	.13	.07	.10	.12	.79**	1		
17. B IPB	.01	.05	-.12	-.02	-.25*	-.18	-.09	.10	.14	.16	.08	-.03	.08	-.03	.40**	.34**	1	
18. FU IPB	-.08	.05	-.15	-.08	-.23	-.20	-.19	-.02	.06	.09	.06	.01	.03	-.05	.35**	.47**	.83**	1

* $p < .05$. ** $p < .01$. B = baseline. FU = follow-up. alc = alcohol use frequency. can = cannabis use frequency. drug = hard drug use frequency. freq = frequency of the each adolescent's most used substance (alc, can, drug). AUD = sum score of Alcohol Use Disorders Identification Test. DUD = sum score of Drug Use Disorders Identification Test. sev = severity score most problematic substance (AUD or DUD). EPB = externalising problem behavior. IPB = internalising problems.

Appendix 2. *Bivariate correlations of study 1 outcome measures separately for intervention and control groups.*

	1.	*2.*	*3.*	*4.*	*5.*	*6.*	*7.*	*8.*	*9.*	*10.*	*11.*	*12.*	*13.*	*14.*	*15.*	*16.*	*17.*	*18.*
1. B alc	1	.17	-.02	.20	.17	.03	.40*	.12	.64**	.19	.18	.08	.29	.11	-.17	-.17	-.18	-.28
2. FU alc	.17	1	-.06	-.08	.15	-.29	.02	.31	.01	.58**	.08	-.13	.08	.01	.26	.28	-.10	.13
3. B can	.17	-.12	1	.73**	.56**	.58**	.76**	.52**	-.04	.19	.48**	.70**	.47**	.46**	.02	-.11	-.08	-.18
4. FU can	.04	-.09	.48**	1	.30	.64**	.62**	.65**	.18	.21	.38*	.82**	.44*	.64**	-.02	-.01	-.07	-.09
5. B drug	.05	-.28	.57**	.16	1	.33	.51**	.28	.06	.52*	.73**	.32	.73**	.48**	.19	.04	-.08	-.11
6. FU drug	-.33	-.18	.23	.49**	.36*	1	.53**	.49*	.09	-.07	.43*	.86**	.45**	.65**	-.04	-.13	-.03	-.14
7. B freq	.42*	.07	.83**	.32	.52**	.18	1	.61**	.28	.16	.62**	.61**	.64**	.48**	-.02	-.15	.02	-.18
8. FU freq	.00	.36*	.06	.61**	-.17	.37*	.15	1	.10	.25	.45**	.70**	.46**	.70**	.06	.01	.13	.09
9. B AUD	.41*	.34*	.20	.10	.14	-.02	.31	.04	1	.43	.14	.14	.31	.25	-.02	-.04	.19	.01
10. FU AUD	-.04	.55**	-.07	-.13	-.13	-.12	-.04	.12	.72**	1	.16	.12	.38	.38	.24	.22	-.24	-.10
11. B DUD	.17	-.10	.65**	.21	.66**	.19	.51**	-.20	.28	.15	1	.65**	.94**	.65**	.21	.09	.24	.11
12. FU DUD	.15	-.23	.48*	.47*	.47*	.66**	.43*	.22	.34	.13	.68**	1	.69**	.85**	.01	-.03	.03	-.02
13. B sev	.38*	.01	.60**	.10	.60**	.08	.60**	-.20	.52**	.33	.91**	.62**	1	.72**	.25	.12	.17	.02
14. FU sev	.22	-.22	.28	.25	.43*	.44**	.29	.14	.38*	.34	.50**	.84**	.59**	1	.21	.08	.10	.02
15. B EPB	.01	.41*	.10	.35*	-.14	-.13	.05	.08	.09	.35	.15	.04	.10	.03	1	.79**	.37*	.56**
16. FU EPB	-.17	.08	.16	.29	-.12	-.08	.01	.12	-.08	.26	.17	.16	.09	.16	.83**	1	.31	.70**
17. B IPB	.17	.20	-.15	.04	-.39*	-.35*	-.20	.07	.21	.39*	-.05	-.10	.01	-.14	.45**	.37*	1	.79**
18. FU IPB	.07	-.02	-.16	-.05	-.36*	-.26	-.24	-.10	.06	.20	.10	-.01	.02	-.13	.21	.23	.88**	1

Bottom left of diagonal = intervention condition. Top right of diagonal = control condition. * $p < .05$. ** $p < .01$. B = baseline. FU = follow-up. alc = alcohol use frequency. can = cannabis use frequency. drug = hard drug use frequency. freq = frequency of the each adolescent's most used substance (alc, can, drug). AUD = sum score of Alcohol Use Disorders Identification Test. DUD = sum score of Drug Use Disorders Identification Test. sev = severity score most problematic substance (AUD or DUD). EPB = externalising problems. IPB = internalising problems.