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Multidimensional family therapy lowers the rate of cannabis dependence in adolescents: A randomised controlled trial in Western European outpatient settings☆

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ABSTRACT

Background: Noticing a lack of evidence-based programmes for treating adolescents heavily using cannabis in Europe, government representatives from Belgium, France, Germany, The Netherlands, and Switzerland decided to have U.S.-developed multidimensional family therapy (MDFT) tested in their countries in a trans-national trial, called the International Need for Cannabis Treatment (INCANT) study.
Methods: INCANT was a 2 (treatment condition) × 5 (time) repeated measures intent-to-treat randomised effectiveness trial comparing MDFT to Individual Psychotherapy (IP). Data were gathered at baseline and 3, 6, 9 and 12 months thereafter. Study participants were recruited at outpatient secondary level addiction, youth, and forensic care clinics in Brussels, Berlin, Paris, The Hague, and Geneva. Participants were adolescents from 13 through 18 years of age with a recent cannabis use disorder. 85% were boys; 40% were of foreign descent. One-third had been arrested for a criminal offence in the past 3 months. Three primary outcomes were assessed: (1) treatment retention, (2) prevalence of cannabis use disorder and (3) 90-day frequency of cannabis consumption.
Results: Positive outcomes were found in both the MDFT and IP conditions. MDFT outperformed IP on the measures of treatment retention ($p < 0.001$) and prevalence of cannabis dependence ($p = 0.015$). MDFT reduced the number of cannabis consumption days more than IP in a subgroup of adolescents reporting more frequent cannabis use ($p = 0.002$).
Conclusions: Cannabis use disorder was responsive to treatment. MDFT exceeded IP in decreasing the prevalence of cannabis dependence. MDFT is applicable in Western European outpatient settings, and may show moderately greater benefits than IP in youth with more severe substance use.

1. Introduction

1.1. Background

In most Western European countries, 3–5% of youth consume cannabis nearly every day (European Monitoring Centre for Drugs and Drug Abuse, 2011). Frequent use of cannabis is associated with concurrent problem behaviour, such as aggression, delinquency, truancy, and mental co-morbidity (Hussong et al., 2005; Monshouwer et al., 2006), as well as lower

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education and life satisfaction levels in the long term (Fergusson and Boden, 2008). There is a lack of evidence-based treatment options for adolescents with cannabis use disorder in Europe (European Monitoring Centre for Drugs and Drug Abuse, 2011).

Western European countries have been disputing their cannabis policies for years. In 2003, the government members for health from Belgium, France, Germany, The Netherlands and Switzerland agreed on priorities for joint research. Top of the list was a treatment programme for adolescent cannabis use disorder. In a systematic literature review (Rigter, 2005b), only a small number of randomised controlled trials targeting cannabis abusing adolescents could be traced. The outcomes of behavioural approaches, such as cognitive behavioural therapy (CBT) and stand-alone motivational enhancement, were mixed. The evidence base was most convincing for multidimensional family therapy (MDFT). The government representatives selected MDFT for a treatment study in Western Europe (Rigter, 2005a), on which we report here.

MDFT is a family-based therapy for adolescent substance abuse and associated problems, developed by Liddle et al. (1991), presently at the University of Miami Miller School of Medicine ('Miami'). MDFT holds that each major domain in the life of an adolescent influences the rise and decline of behavioural problems. These life domains include the youth, parents and extended family, peers, school and work and leisure time. MDFT views family functioning as instrumental in creating adaptive lifestyle alternatives for the adolescent in each of these domains.

1.2. Objectives

So far, MDFT has been found effective in eight randomised trials, all carried out in the USA (Liddle, 2010). Our objective was to evaluate MDFT with Western European adolescents, in a transnational trial (INCANT). Of issue was the transferability of MDFT to Europe, the applicability of MDFT in diverse treatment settings and in heterogeneous samples of adolescents.

We wanted to compare MDFT with an active treatment from the 'treatment as usual' (TAU) repertoire in the participating clinical sites. The predominant TAU approach in all INCANT sites was working with just the adolescents in individual sessions (Rigter, 2005a). We selected this form of TAU as the comparison treatment, and labelled it 'individual psychotherapy' (IP). From meta-analyses (Austin et al., 2005; Baldwin et al., 2012; Bender et al., 2011; Waldron and Turner, 2008), we know that versions of IP may decrease cannabis use in adolescents, especially if based on cognitive behavioural principles and/or including motivational enhancement (Miller and Rollnick, 2002) sessions. Based on the cited meta-analyses, we expected MDFT and IP to decrease the number of days of cannabis use. We assumed that MDFT would do better on this measure than IP in the most heavily cannabis using adolescents, as has been found earlier when MDFT was compared with CBT (Henderson et al., 2010).

Self-reported number of days of cannabis use is the most common outcome measure in cannabis treatment research, but it does not tell if the adolescent is free of cannabis use disorder (symptoms). Therefore, we included distal outcome measures in the trial, i.e., the prevalence of cannabis use disorder at symptom and diagnosis levels, expecting MDFT to outperform IP here without having hard evidence at hand: surprisingly, cannabis use disorder diagnosis has rarely been used as an outcome measure. We also examined the number of cannabis dependence symptoms, as it is not just diagnosis that matters, but also the severity of the constituting symptoms (Saha et al., 2012).

1.3. Funding

This research was funded by the (federal) Ministries of Health of Belgium, Germany, The Netherlands, Switzerland, and by MILDT: the Mission Interministerielle de Lutte Contre la Drogue et de Toximanie, France. These agencies had no influence on the design and the execution of the study, or on the interpretation and reporting of its results.

2. Methods

2.1. Approval and monitoring

INCANT was approved by the Ethical Board of Brugmann University Hospital (Belgium), the Chamber of Psychological Psychotherapists and Child and Adolescent Therapists in Berlin state (Germany), the Hotel-Dieu Committee for the Protection of Human Subjects in Biomedical Research (France), the medical–ethical committee METiGG (The Netherlands), the Ethical Board for Clinical and Outpatient Research (Medical Association Geneva Canton, Switzerland), and by the Institutional Review Board (IRB) of the University of Miami Miller School of Medicine in the USA. The International INCANT Study Team (IST) and the IRB oversaw the conduct of the trial.

2.2. Design

INCANT was a multi-centre phase III(b) randomised controlled effectiveness trial with an open-label, parallel group design. Study sites started the 24-month recruitment phase between July 2006 and February 2007. Assessments were scheduled at baseline, immediately before randomisation, and at 3, 6, 9 and 12 months thereafter.

2.3. Participants

Eligible participants were boys and girls from 13 through 18 years of age, with a cannabis use disorder (dependence or abuse) established for the past year at baseline, and with at least one parent willing to take part in the treatment. Cannabis use disorder was determined following DSM-IV guidelines, with dependence being diagnosed if at least 3 of 7 dependence criteria had been met, and abuse if at least 1 of 4 abuse criteria had been met.

Adolescents were ineligible if they suffered from a current mental disorder or condition (psychosis, advanced eating disorder, suicide ideation) requiring inpatient treatment or had a substance use disorder requiring maintenance treatment with methadone or buprenorphine. Cases were excluded if the adolescent and/or parent were unable to speak and read the local language.

Baseline assessment was scheduled in two meetings. In the first, the focus was on need for treatment. When the assessor thought the case might meet INCANT inclusion criteria, she explained the study and allowed the family time to consider giving informed consent. Cases (adolescent plus parent) were excluded if one or both did not show up for the second meeting, not even after prompting (Fig. 1). The presence of a cannabis use disorder (adolescent) was confirmed in the second meeting.

The adolescents were remunerated for completing follow-up assessments, for a total of € 60–70 accumulated across the follow-up assessments, except for France, where rewarding of study participants is forbidden.

2.4. Study sites

Sites were selected from secondary level addiction, youth and forensic care centres upon nomination by government officials,

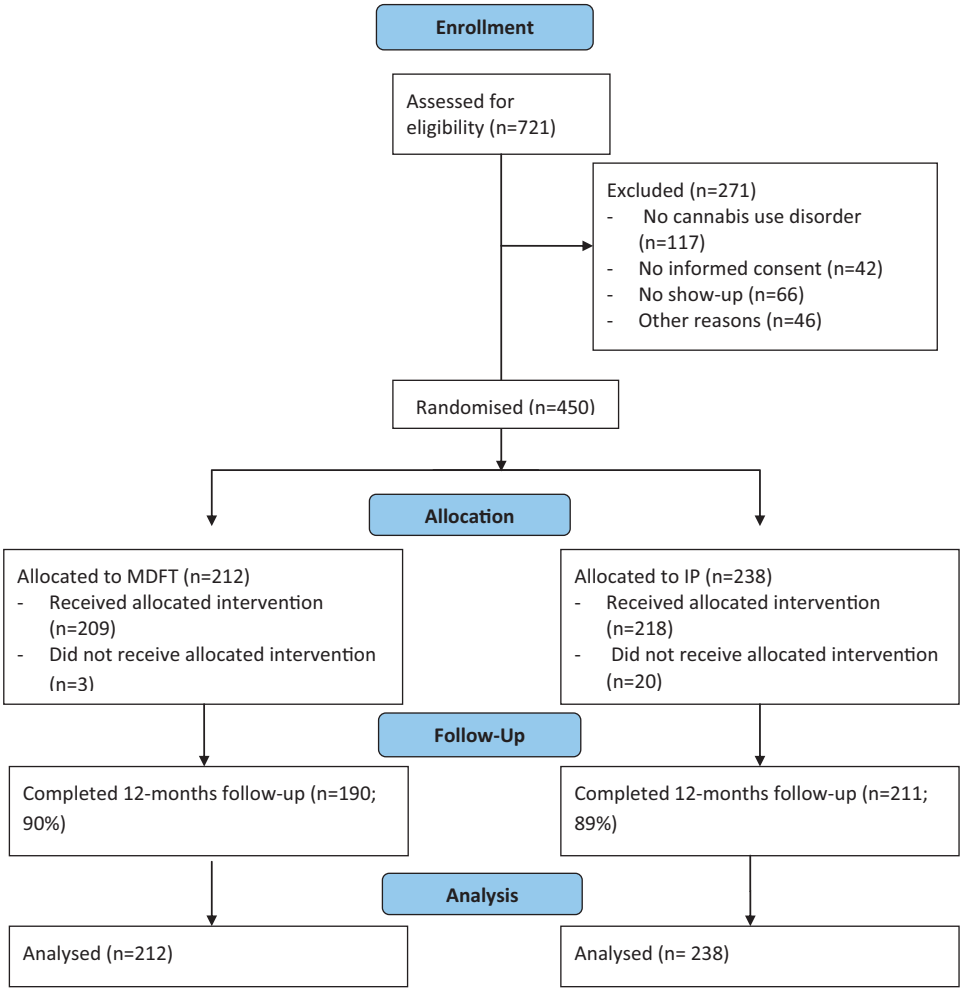

Fig. 1. Trial flow diagram.

after site visits by study staff, and on the basis of performance in a pilot study. The sites were (a) The Outpatient Cannabis Clinic of The Department of Psychiatry of Brugmann University Hospital in Brussels, (b) Therapieladen in Berlin, (c) Centre Emergence in Paris with suburban CEDAT (Conseils Aide et Action contre le Toximanie) sub-sites in Mantes la Jolie and St. Germain en Laye, (d) the twinning sites of Parnassia Brijder (addiction care) and De Jutters (forensic care) in The Hague, and (e) Phénix in Geneva (Rigter, 2005a). All sites were youth oriented; see Table 1 for details on the treatment agencies concerned. In a pilot study preceding INCANT, the recruitment potential for INCANT was confirmed, and therapists appeared to be trainable in MDFT (Rigter, 2005a).

2.5. Randomisation and masking

Concealed randomisation occurred immediately after the eligibility of the case had been confirmed in the second baseline meeting. The database assigned a code to each new case entered by a research assessor and automatically informed her about the allocated treatment, independently from any trial staff. The allocation ratio for MDFT and IP was 1:1, except in Paris (1:2) where

Table 1
Characteristics of INCANT sites.

Site	Treatment sector	Location	Public or private
Belgium	Addiction care; mental health care	Brussels University affiliated outpatient clinic	Public MDFT funded by the federal government
France	Addiction care	Paris and suburbs Part of national addiction treatment infrastructure	Public MDFT funded by the federal government
Germany	Addiction care and youth care	Berlin Part of regional (state level) addiction treatment infrastructure	Public MDFT funded by federal and local governments
The Netherlands	Addiction care Forensic youth care	The Hague Part of national and regional addiction and forensic treatment infrastructures	Public Reimbursed by health insurance funds
Switzerland	Addiction care	Geneva Part of regional addiction and forensic treatment infrastuctures	Public - private mix Mostly reimbursed by health insurance and social funds

manualised and a non-manualised IP were examined (collapsed in this paper into one IP condition). We stratified the study sample per site using three dichotomous variables (gender, age [13–14 years vs. 15–18 years], and level of cannabis use in the past 90 days [74 or fewer days of cannabis consumption vs. 75 or more]). For each stratum, the database computer generated 50 independent randomisations.

Once notified of the treatment, the research assessor informed the case and the site's therapist being 'next in line' for accepting a new MDFT or IP case. As a rule, families were introduced to the therapist right after randomisation. Treatment started within one month (median: 15 days) of randomisation. Therapists could not be blinded to the treatment. Research staff were unaware of treatment condition when carrying out assessments and analysing outcomes.

2.6. Therapists and interventions

Different therapists from the same site delivered MDFT and IP. MDFT ($n = 21$) and IP therapists ($n = 20$) were similar in experience in treating adolescents (from 3 to 20 years). On average, they were 39.6 years old, and 66% were female, with no differences between treatment conditions (Rowe et al., 2012). All worked as psychotherapist and had advanced degrees in psychology or psychiatry, counselling, or social work.

Selection of the site's MDFT supervisor was by site visit interview and follow-up correspondence. The MDFT therapists to be selected were immediate colleagues of the supervisor candidate. MDFT developers from Miami trained the European MDFT teams, according to the Miami training model and the MDFT manual (Rowe et al., 2012). Training started 2 years before the INCANT trial, with four separate weeks of joint intensive didactic training in Europe, followed by several site-specific visits conducted by Miami trainers annually, also during INCANT, for case review, examination of exemplary MDFT sessions, role playing, and review of recorded therapy sessions. Throughout the pilot study and INCANT itself, the Miami trainers held consultation calls twice a month with each European team, discussing progress of cases and results from session recordings and treatment contact logs submitted by team members (Rowe et al., 2012). In INCANT sites, all therapists in both conditions were internally supervised.

In the trial, a mean of two MDFT sessions per week was prescribed, in roughly equal proportion to be held with the adolescent, parent, and family (adolescent and parent together), respectively. Sessions could take place at the office of the therapist, the family's home, or any other location. IP was to last as long as MDFT (6 months), but with fewer sessions per week. Rowe et al. (2012) report details on the actual treatment dose received.

IP was individual counselling of the adolescent, which was treatment as usual across sites. IP was not standardised across sites, and varied from full CBT in The Hague (Hendriks et al., 2011) and predominantly CBT in Brussels, to more elective approaches in the other countries involving CBT but also (especially in Paris and Geneva) psychodynamic principles. IP always included motivational interviewing. MDFT and IP were similar in administrative procedures such as holding regular therapist supervision meetings, and communicating with referral sources and authorities. MDFT and IP both incorporated drug education and focused on substance use triggers and strategies for relapse prevention (Rigter et al., 2010). In INCANT, IP was to exclude sessions with the parents or the family, except for informative meetings with parents once a month, and this was achieved (Rowe et al., 2012).

INCANT therapists submitted data on the number, duration, spacing, and participants of sessions. MDFT therapists also submitted recordings of one family session for every fourth MDFT case ($n = 153$ tapes) for review by independent raters (cf. Hogue et al., 1998). Research staff monitored session logs and recordings throughout the trial. European MDFT therapists showed fidelity to MDFT (Rowe et al., 2012).

2.7. Outcome measures

Primary outcomes were related to cannabis use. All adolescents had a cannabis use disorder in the year before baseline as assessed by the Adolescent Diagnostic Interview-Light (ADI-Light for cannabis). This interview provides both DSM-IV based cannabis use disorder symptoms and cannabis use disorder diagnoses. The ADI-Light has strong psychometric properties (Winters and Henly, 1993). It was administered at baseline and at 12-month follow-up. Another outcome measure was frequency of cannabis use, recorded with the timeline follow-back method (TLFB) for adolescents (Waldron et al., 2000). The TLFB obtains reports of daily cannabis use for the 90 days preceding the assessment, using a calendar and other memory prompts.

2.8. Statistical analyses

We used an intent-to-treat approach, with outcome change over time analysed with latent growth curve modelling (LGC; Muthén and Muthén, 2000). For cannabis use disorder diagnoses, we examined change in the proportion of participants meeting diagnostic criteria from baseline to the 12 month follow-up, using Mplus algorithms for categorical data and fixing the variance of the slope parameter to zero to enable model identification. Further, we modelled cannabis dependence symptoms as count data applying Mplus algorithms (Muthén and Muthén, 1998–2012). We included site and referral source (self-directed or externally coerced referral) as covariates, based on INCANT's baseline findings (Phan et al., 2011). Site by treatment interactions were not statistically significant (Cohen's d effect sizes were 0.06 for cannabis dependence and 0.05 for the TLFB), and therefore were omitted from the final models. Missing data were handled with full information maximum likelihood estimation, under the missing at random assumption (Little and Rubin, 1987). A statistically significant ($p < 0.05$) slope parameter, as tested by the pseudo-z test, indicated the intervention was effective. We calculated between-treatment effect sizes (Cohen's d) with a method adapted for LGC modelling (Feingold, 2009). Because MDFT participants were retained in treatment longer than IP participants (see below), we included time in treatment (total hours of session time) as a covariate in our LCG models.

For TLFB data, we analysed an adolescent's individual change in cannabis consumption rate, also using LGC modelling with robust maximum likelihood estimation. In earlier studies, MDFT was more effective than CBT especially in adolescents with more severe substance use (Henderson et al., 2010). Therefore, in addition to change in frequency of substance use over the entire sample, we also examined treatment differences within sub-samples with TLFB scores below and above the median (cf. Hendriks et al., 2011). For simple group comparisons we used the χ^2 test for categorical and analysis of variance (ANOVA) for continuous data.

3. Results

3.1. Trial profile

Fig. 1 shows the trial flow diagram. Of 721 adolescents seen, 16% did not have a cannabis use disorder. Less than 6% of cases (adolescents and/or parents) refused to give informed consent. Baseline assessments were scheduled across two meetings; 9% of cases did not show up for the second meeting. 6% of cases were not enrolled for other reasons, such as the referral authority not accepting the randomisation process, and, infrequently,

because of language barriers or because the adolescent needed inpatient treatment.

We randomised 450 cases, i.e., 60 from Belgium (30 MDFT, 30 IP), 101 from France (38 MDFT, 63 IP), 120 from Germany (59 MDFT, 61 IP), 109 from the Netherlands (55 MDFT, 54 IP), and 60 from Switzerland (30 MDFT, 30 IP). The lower number of cases to be recruited in Belgium and Switzerland followed from budget limitations. As for the excluded cases, χ^2 and ANOVA tests found them to be similar to the included cases in age, gender and level of cannabis use.

There was limited pre-treatment dropout from the study after cases had been informed of the assigned therapy. Across sites, such dropout happened in 3 MDFT and 20 IP cases ($\chi^2[4, n = 450] = 11.3$, $p = 0.001$). Dropout was caused by the youth absconding, or by second thoughts among family members about the desirability of treatment. All randomised dropout cases were maintained in the intent-to-treat analyses. They did not stand out in terms of age, gender, and level of cannabis use (MDFT + IP pre-treatment dropout cases combined vs. all other cases, χ^2 tests, *ns*). Outcome analyses including or excluding the data from the dropout cases were very similar (see Supplementary Material).

The across-site 12-month follow-up completion rate was 89%, with Belgium somewhat lagging behind (70%) and other sites achieving a rate between 90% and 94% (no statistical differences between sites). Averaged across sites, intermediate follow-up completion rates were 87% at 3-month, 81% at 6-month, and 78% at 9-month follow-up. Intermediate follow-up completion rates were close to or above 90% in all sites, except in the Netherlands (65% completion at 3 months, 54% at 6 months, 50% at 9 months) and Belgium at 9 months follow-up (63%). The low Dutch rates were due to long-term illness of key site staff members. The rate in The Hague improved greatly at 12 months (94%). Averaged across sites, the cases with missing 12-month follow-up data did not statistically differ from the other cases on baseline demographic and primary outcome variables.

3.2. Across-site baseline characteristics

The mean age of the adolescents was 16.3 years; 85% were boys. 40% was of first- or second-generation foreign descent (Phan et al., 2011). In total, 84% was dependent on cannabis, with differences between sites, from close to 80% in Paris and The Hague to well over 90% in Brussels and Geneva, with Berlin in between (The INCANT Study Team, 2011). Four in ten had an alcohol use disorder. Substance use disorders for drugs other than cannabis were rare (<5%). Most adolescents lived with their family (87%) and attended school (75%). Parents were divorced or separated in 56% of cases. One in three adolescents had been arrested in the past three months, mostly for drug offences, property crimes, and violence. MDFT and IP groups did not differ on these variables, with a single exception (MDFT Brussels condition: more adolescents of foreign descent than in the corresponding IP condition).

3.3. Treatment retention and treatment contrast

MDFT retained cases in treatment more effectively than IP (Rowe et al., 2012). For each case, we asked the therapists to rate if the treatment had been properly completed. MDFT therapists said that 90% ($n = 179$) of their cases had completed therapy, a higher proportion than reported by IP therapists (48%; $n = 98$) ($\chi^2[1, n = 404] = 83.2$, $p < 0.001$; OR = 9.8 [95% CI = 5.7–16.7]). MDFT completion rates were similar across sites, but IP completion rate differed ($\chi^2[4, n = 205] = 32.0$, $p < 0.001$), with Germany and Switzerland having the highest retention rates. On another measure, at least 3 months of treatment completed, a benchmark for treatment success commonly used in adolescent drug abuse treatment studies (Hser et al., 2001), MDFT also exceeded IP (95% vs. 73%) ($\chi^2[1, n = 401] = 34.7$, $p < 0.001$; OR = 6.8 [95% CI = 3.4–13.8]; Rowe et al., 2012).

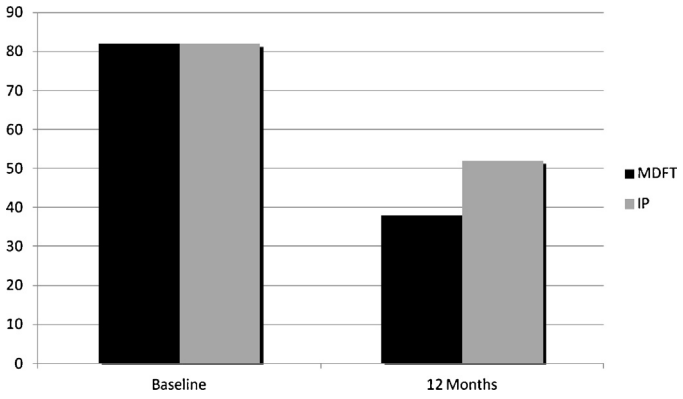

Fig. 2. Proportion (%) of adolescents presenting with cannabis dependence diagnosis across sites, at baseline and 12-month follow-up. MDFT, multidimensional family therapy; IP, individual psychotherapy.

3.4. Diagnosis of cannabis use disorder

The prevalence rate of cannabis use disorders (dependence and abuse combined) declined from 100% at baseline to 71% (MDFT) and 74% (IP) at 12-month follow-up (*ns* between treatments: χ^2 [1, $n = 401$] = 1.0).

A drop in overall prevalence level was also seen when examining the most common diagnosis, cannabis dependence (total sample slope = −1.9 [95% CI = −2.3 to −1.5], pseudo-z = −8.4, $p < 0.001$; Fig. 2 and Table 2). At 12-month follow-up, 38% of MDFT adolescents met the criteria for cannabis dependence and 33% for cannabis abuse, with 18% no longer having a cannabis use disorder. In IP, the corresponding numbers were 52%, 22%, and 15% (these percentages pertain to all cases including those with missing values at follow-up, so do not add up to 100%). This finding suggests a shift from dependence to less severe conditions, namely, abuse or no disorder. LGC modelling indicated this shift was greater for MDFT than for IP (differential slope coefficient on treatment =

Table 2
Number and proportion of adolescents presenting with recent cannabis dependence diagnosis, by site. Results at baseline and at 12-month follow-up.

Site	Baseline (a)	12 Months (b)	Difference a-b
	N (%)	N (%)	
Belgium			
MDFT	29 out of 30 (97%)	13 out of 30 (43%)	54%
IP	28 out of 30 (93%)	12 out of 30 (40%)	40%
France			
MDFT	29 out of 38 (76%)	13 out of 38 (34%)	42%
IP	46 out of 63 (73%)	24 out of 63 (38%)	35%
Germany			
MDFT	51 out of 59 (86%)	26 out of 59 (44%)	42%
IP	55 out of 61 (90%)	43 out of 61 (71%)	19%
Netherlands			
MDFT	37 out of 55 (66%)	16 out of 55 (29%)	37%
IP	37 out of 54 (69%)	30 out of 54 (56%)	13%
Switzerland			
MDFT	28 out of 30 (93%)	13 out of 30 (43%)	50%
IP	29 out of 30 (97%)	15 out of 30 (50%)	47%
Total			
MDFT	173 out of 212 (82%)	81 out of 212 (38%)	44%
IP	195 out of 238 (82%)	124 out of 238 (52%)	30%

Note. MDFT = Multidimensional Family Therapy, IP = treatment as usual, N = number.

Table 3
Mean number of self-reported days of cannabis use in the past 90 days, by site.

Number of days	Baseline	3 Months	6 Months	9 Months	12 Months
	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)
Belgium					
MDFT	68·4 (20·6)	52·3 (30·6)	51·1 (30·4)	46·7 (27·3)	42·5 (29·6)
IP	66·7 (23·1)	60·4 (27·5)	59·7 (29·5)	52·7 (29·1)	62·2 (31·5)
France					
MDFT	60·2 (24·7)	38.0 (31·5)	39·5 (34·8)	36·6 (36·1)	30·9 (32·8)
IP	63·2 (26·8)	46·4 (31·1)	36·2 (29·9)	41·2 (32·9)	35·2 (29·1)
Germany					
MDFT	58·8 (28·2)	26·4(30·5)	20·1 (27·1)	21·6 (29·5)	21·3 (27·1)
IP	62·3 (24·1)	37·5 (27·0)	35·3 (29·0)	32·6 (30·0)	36·7 (33·6)
The Netherlands					
MDFT	62·6 (22·7)	44·1 (32·5)	37·0 (29·9)	48·1 (34·3)	42·4 (34·2)
IP	60·9 (23·7)	47·1 (32·3)	46·4 (32·0)	47·9 (29·3)	49·0 (34·1)
Switzerland					
MDFT	47·3 (25·0)	47·2 (32·6)	34·5 (31·7)	34·8 (32·6)	39·3 (35·1)
IP	52·2 (29·5)	44·9 (31·1)	44·7 (36·1)	42·3 (35·8)	39·3 (36·9)
Total					
MDFT	59·8 (25·3)	39·4 (32·5)	33·9 (31·9)	35·0 (33·5)	34·0 (32·6)
IP	61·5 (25·4)	45·2 (30·2)	41·8 (31·6)	40·8 (32·0)	42·3 (33·8)

Note. MDFT = Multidimensional Family Therapy, IP = treatment as usual, M = mean, SD = standard deviation.

0.9 [95% CI = 0.2–1.7], pseudo-z = 2.4, p = 0.015, d = 0.65). Treatment difference on this measure was largest in The Hague (d = 1.03), moderate in magnitude (d = 0.5 or slightly higher) in Paris and Berlin, small in Brussels and virtually absent in Geneva. The treatment difference in The Hague was statistically significant; see within-site outcomes in Supplementary Material. When time in treatment was included as a covariate, the treatment difference was no longer significant (overall differential slope coefficient on treatment = 0.8 [95% CI = −0.3 to 1.8], pseudo-z = 1.5, p = 0.145), but the corresponding effect size was still moderate (d = 0.52).

3.5. Symptoms of cannabis dependence

Next, we turned to cannabis dependence symptoms, counting the number (maximum 7) of symptoms. At baseline, MDFT and IP adolescents reported an average of 4.1 (SD = 1.7) and 4.0 (SD = 2.0) dependence symptoms, respectively. Across sites and therapy conditions, both treatments decreased the number of dependence symptoms from baseline to 12-month follow-up (total sample slope = −0.4 [95% CI = −0.5 to −0.3], pseudo-z = −11.0, p < 0.001). The 12-month symptoms average was 2.4 for MDFT (SD = 2.0) and 3.0 for IP (SD = 2.0). The drop in symptoms was larger in MDFT than in IP (differential slope coefficient on treatment = 0.27 [95% CI = 0.13–0.41], pseudo-z = 3.7, p < 0.001, d = 1.27). MDFT most strongly diminished the number of cannabis dependence symptoms in Berlin (d = 1.76) and The Hague (d = 1.29), followed by Geneva (d = 0.76), Paris (d = 0.76), and Brussels (d = 0.41). We reran the model including time in treatment as a covariate, and the results remained statistically significant (differential slope coefficient on treatment = 0.35 [95% CI = 0.15–0.55], pseudo-z = 3.4, p = 0.001, d = 1.66).

3.6. Frequency of cannabis use

On average, adolescents had taken cannabis on 61 (standard deviation SD = 25.3) out of 90 days before the baseline assessment, with no differences between sites and treatment conditions. Both treatments reduced the number of cannabis consumption days across assessments (total sample slope = −5.0 [95% CI = −6.0 to −4.1], pseudo-z = −10.3, p < 0.001; Table 3 and Fig. 3). This was true of all sites. At 12-month follow-up, the mean number of consumption days had decreased by 43% (35 days) in MDFT and by 31% in IP. This difference was not statistically significant (differential slope coefficient on treatment = 1.6 [95% CI = −0.2 to 3.3], pseudo-z = 1.8, p = 0.07, d = 0.25).

We divided each treatment group in high-severity (above a group's TLFB median number of consumption days) and low-severity cannabis users (below the median). The high-severity MDFT group reduced the frequency of cannabis consumption more across assessments points than the corresponding IP group did (differential slope coefficient on treatment = 3.8 [95% CI = 1.4–7.6], pseudo-z = 3.1, p = 0.002; d = 0.60). The high-severity effect was also seen at the individual site level, except in Paris (Brussels d = 0.58, Berlin d = 0.84, The Hague d = 0.81, Geneva d = 1.35, Paris d = 0.19).

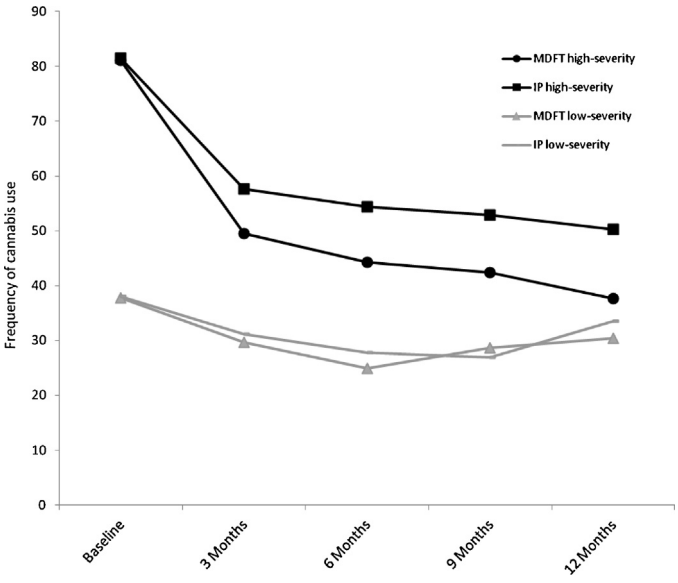

Fig. 3. Trajectories of mean number of cannabis consumption days during the 90 days preceding baseline and follow-up assessments. High-severity and low-severity = above- and below-median number of consumption days at baseline, respectively. MDFT, multidimensional family therapy and IP, individual psychotherapy.

The low-severity MDFT and IP groups did not differ from each other (across sites $p = 0.71$).

Adjusting for hours of treatment, effects diminished for treatment differences overall (differential slope coefficient on treatment = −0.5, pseudo-z = −0.4, *ns*, $d = 0.11$), for high severity (differential slope coefficient on treatment = 1.6, pseudo-z = 0.9, *ns*, $d = 0.32$), and for low severity groups (differential slope coefficient on treatment = −0.9, pseudo-z = −0.6, *ns*, $d = 0.18$).

4. Discussion

4.1. Key findings

MDFT retained cases better in treatment than IP. MDFT outperformed IP in reducing the prevalence of cannabis dependence disorder and symptoms, across sites and, in general, within sites. MDFT and IP did not differ in 12-month follow-up cannabis disorder rate (18% of MDFT adolescents and 15% in IP with no such disorder). MDFT was more successful than IP in moving adolescents from dependence to abuse, but did not free them from all cannabis trouble. In both MDFT and IP, the number of cannabis consumption days decreased. On this measure, MDFT did better than IP in the 'high-severity' cannabis consumption group.

4.2. Strengths of the study

INCANT was carried out semi-independently from the Miami developers. The developers trained MDFT therapists, but had no role in the actual execution of the research study. Among the strengths of the trial are the multinational effort, the importance of using cannabis use disorder as an outcome measure, the good follow-up rates, and the use of advanced analytic techniques.

4.3. Comparison across INCANT sites

Across sites, cases were similar on demographic variables. As reported earlier (Phan et al., 2011), sites differed in the way adolescents were referred. Reflecting varying societal views on proper youth care policies, referral by family and friends and self-referral were more common in Brussels and Paris than in Berlin and The Hague, where professional agencies carried more weight and in Geneva with its high proportion of referral by Justice-related authorities. We included referral source in our present analyses, but this variable did not affect outcomes.

In both the MDFT and IP condition, irrespective of site, the number of days of cannabis consumption, the number of cannabis dependence symptoms, and the prevalence of cannabis dependence declined. MDFT was superior to IP on treatment retention also irrespective of site. On the outcomes where MDFT led to greater reductions, results collapsing across sites were mostly confirmed in individual sites. In all sites except for Paris, MDFT was superior to IP on the number of cannabis use days in high-severity users. In all sites, MDFT reduced the number of cannabis dependence symptoms more strongly than IP. In all sites except for Brussels and Geneva with their small samples, MDFT was superior to IP in moving adolescents from cannabis dependence to cannabis abuse or the non-disorder state.

The concordance of treatment outcomes across sites is worth mentioning. The five countries from where we selected our sites differed on treatment policy issues such as case referral, reimbursement for therapy, and academic route towards qualifying as a psychotherapist. One might expect such differences to obscure treatment effects, but they did not. Note, though, that we compared European sites, not the countries themselves. What is true for Berlin or Paris, etc., may not be true for all of Germany or France.

4.4. The comparison treatment

As comparison treatment, we selected the most common form of TAU, which was individual psychotherapy for the adolescent, with very limited parent involvement in the therapy. Although 'individual psychotherapy' is a proper label for all our sites, sites differed in orientation of IP. Yet, IP always included motivational interviewing and at least some input from cognitive behavioural therapy (CBT).

That sites differed in IP may be seen as a study limitation, but variability of IP could also be viewed as an advantage. The aim of INCANT was to test the usefulness of MDFT in a study with high external validity, and as such, we sought to compare MDFT to treatment as currently delivered in a site. INCANT shared this emphasis on external validity with for instance trials implemented by the National Institute on Drug Abuse Clinical Trials Network (e.g., Robbins et al., 2011).

The therapists offering MDFT and IP were similar in age, gender and clinical experience. They were not allocated randomly to treatment condition. Conceivably, the INCANT MDFT therapist selection process might have resulted in assigning better/different therapists to the MDFT branch than to the IP branch. We are sure that such bias, if present, was small. After conclusion of INCANT, almost all INCANT IP supervisors and therapists applied for training in MDFT. MDFT quality assurance records show them to do as well as their INCANT MDFT colleagues.

The performance of MDFT therapists was monitored through treatment session recordings and by other means. INCANT imposed no such monitoring on IP therapists. One might say that the MDFT condition was advantaged by the monitoring procedures. However, sites had monitoring mechanisms and protocols in place for IP for quite some time (to be reported), and therefore did not need the initial monitoring MDFT therapists were exposed to when trained in this novel treatment programme. The MDFT monitoring in INCANT was meant to support therapy training, not to structure daily practice. Nevertheless, MDFT and IP therapist conditions were not identical in monitoring procedures.

We could not match 'time in treatment' between the MDFT and IP conditions. MDFT includes sessions with parents, family, and representatives of systems outside the family, which are excluded from IP. Besides, MDFT retained cases much better in treatment than IP did, meaning that treatment dose was higher in the MDFT condition. When adjusting cannabis dependence data for differences in 'time of treatment', MDFT treatment effect relative to IP remained statistically significant for the cannabis dependence symptom count data, but no longer for the diagnosis data. Therefore, time in treatment had some impact on treatment outcomes, along with the type of treatment the youth received.

4.5. Comparison with other studies

Treatment trials for cannabis use disorders in European adolescents have been rare. Most studies concerned youth taking cannabis without having established cannabis use disorder. Furthermore, most studies targeted substance abuse (drugs and alcohol), rather than consumption of just cannabis, making it difficult to parcel out a treatment effect on cannabis use. Earlier studies on cannabis using adolescents have addressed outcome measures such as the number of days of cannabis consumption as measured by the TLFB, and the number of cannabis dependence symptoms. Many interventions tested had some positive effect, even if delivered in a few sessions (Austin et al., 2005; Baldwin et al., 2012; Bender et al., 2011; Waldron and Turner, 2008). Apparently, cannabis use is sensitive to a variety of interventions. Systemic treatments, including MDFT, rank high in evidence classifications in the meta-analyses cited.

Were the treatment effects in INCANT clinically significant? Both treatments were associated with positive outcomes. The effect sizes presented in this paper pertain to the additional effect of MDFT relative to the comparison treatment. Effect sizes were in the medium to high range, with $d = 0.65$ for decreasing cannabis dependence, $d = 1.27$ for diminishing cannabis dependence symptoms, and $d = 0.60$ for reducing the number of cannabis use days in high-severity users. In an analysis of two American trials comparing MDFT to CBT, treatment differences favouring MDFT were $d = 1.54$ for cannabis consumption days among high-severity users in one trial and $d = 0.64$ in a second one (Henderson et al., 2010), similar to what we observed in a far more heterogeneous sample of adolescents.

4.6. Other limitations of the trial

The follow-up period (12 months from randomisation) was relatively short. The value of MDFT is known to become more manifest with longer follow-up periods (Henderson et al., 2010). Unfortunately, our funds did not permit us to extend the follow-up period beyond 12 months.

We included adolescents who had a 'recent' cannabis use disorder as established at baseline, i.e., covering the past year. One might object that the disorder measured was 'past history', and not current anymore. This is not likely. On average, the adolescents had taken cannabis on 61 days in the 3 months before baseline assessment. Tests of urine samples collected at baseline (optional; we have data for 68% of all adolescents) showed that the vast majority had used cannabis recently.

In both MDFT and IP conditions, all primary outcome measures showed that adolescents did better at 12-month follow-up than at baseline. In the absence of a control group receiving no treatment at all, we cannot conclude that the improvement noted was more than could be expected by the passing of time. We did not include such a control group in INCANT for ethical reasons, withholding treatment to youth who after long hesitation or under pressure had sought help, was not an option. MDFT did do better than IP on a number of measures. This suggests that MDFT was more effective than IP, without proving IP to be effective itself.

4.7. Implications for daily practice

Substance use disorder is likely to persist in youth starting to take drugs or drink alcohol early in adolescence (Hussong et al., 2005). INCANT is among the first studies suggesting there may be effective treatment options for (European) adolescents with such disorder. In the present study both treatment approaches examined did matter, but MDFT was the better option in terms of reducing cannabis dependence diagnosis and symptoms rates.

IP was similar across our five sites in including motivational enhancement (interviewing) and excluding family sessions. Nevertheless, there were differences, mostly in the degree of CBT content of IP. CBT has a rather good evidence record in meta-analyses (Austin et al., 2005; Baldwin et al., 2012; Bender et al., 2011; Waldron and Turner, 2008). We found no evidence that IP did better when CBT content was larger; this is an issue that needs to be examined more closely in additional analyses.

Neither MDFT nor IP made most adolescents abstain from using cannabis. This is a general finding according to the meta-analyses just cited. We do not know if the achieved reduction in days of cannabis consumption was substantial or not by lack of reference data, as to our knowledge no European cannabis treatment trials have been carried out with a comparable sample of adolescents with not just a cannabis use disorder, but mostly with other problems as well. Anyway, complete abstinence was not a goal of either treatment approach. Rather, the focus was on reducing the negative consequences of cannabis use. MDFT outperformed IP in this respect by more strongly, albeit modestly, reducing cannabis dependence and cannabis dependence symptoms rate.

MDFT is labour intensive. For financial reasons, this therapy may not be indicated for all adolescents with cannabis use disorder. When cannabis use disorder is mild, interventions labelled as IP may be appropriate alternatives to MDFT. However, when cannabis use is heavy and cannabis dependence is severe or (to be reported) associated with mental co-morbidity or family dysfunction, MDFT would appear to be the treatment of choice.

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Nothing declared.

Contributors

The principal investigator (HR) and CR designed the study. The statistical analysis plan was written by CH. Design of the trial was further developed by the trial management group (INCANT Study Team, IST) of which all authors except CH were member (chair: HR). HR committed the funding agencies to providing financial support for the study. IP, PT, OP, VH and MS (as successor of Prof. J. Rehm) ensured that local funding was granted. They also made sure that local study conditions conformed to the overall INCANT study protocol. All authors were instrumental in obtaining the approval of the respective medical ethical committees. HR and CR trained sites' research assistants in contacting cases for follow-up assessments, in administering questionnaires and interviews, and in entering data into the INCANT database. CR trained INCANT MDFT therapists, and she evaluated their adherence to the MDFT manual. All authors oversaw proper data collection in their respective countries. CH carried out all statistical analyses. HR drafted the manuscript with the assistance of CH. All authors critically reviewed the text, the data and the interpretations. All have approved the present publication, by providing a signed form

Conflict of interest

No conflict declared.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.drugalcdep.2012.10.013.

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