

Differences between men and women in the course of opiate dependence: is there a telescoping effect?

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Abstract According to the so-called telescoping effect, there is a gender-specific course of alcohol dependence with women starting alcohol use later than men and having a faster development of harmful consequences. There are inconsistent data regarding a telescoping effect in opiate dependence. In each of six European centres, 100 opiate addicts were investigated by a structured interview (mainly the EuropASI and CIDI) at admission to various kinds of

treatment (TREAT project). In a secondary analysis of the TREAT data, women and men were compared regarding age at onset of heroin use and the current severity of addiction. In addition, a comparison of female ($n = 140$) and male ($n = 140$) addicts matched for age and study centre were carried out. Eventually, multiple logistic and linear regressions were done with the interaction term of gender and time of regular consumption as predictor for the severity of dependence, besides, other sociodemographic variables. There was no difference between genders regarding the age at onset of regular heroin consumption. Up to 4 years of regular consumption, there are gender-specific differences in the course of opiate dependence, e.g. a faster progression of legal problems in men and social problems in women. There were no differences in the severity of dependence other than more economic problems for women. A telescoping effect could only partially be observed in this large sample of opiate addicts. A gender-specific course was limited to the first years of consumption, and included domains with a faster progression for men. It has to be assumed that opiate dependence is a rapidly developing disorder with early chronification. Afterwards, only individual courses with influences of the national treatment system were observed.

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Background

According to the so-called telescoping effect, there is a gender-specific course of alcohol dependence. Central features of the telescoping effect are that women start later with alcohol use [20] than men, but developed earlier and

more severe harmful consequences than men, especially regarding physical sequelae such as brain atrophy [2, 17]. In addition, women go earlier into first treatment than men [23]. The telescoping effect could be replicated in international studies (e.g. [4, 25]).

There are few and contradictory data for a telescoping effect in opiate dependence. Hernandez-Avila et al. [8] showed a telescoping effect for a heterogeneous sample of 271 patients (156 women) with alcohol, cannabis, cocaine, or opiate addiction entering inpatient or outpatient treatment. In this study, women had more psychosocial and medical problems. In addition, the data of a subsample of opiate addicts ($n = 93$) were analysed. In this subsample, women were overrepresented (women $n = 58$, men $n = 35$) and reported a shorter duration of time between starting regular opiate consumption and first therapy of opiate addiction. Hser et al. [1, 9, 10] analysed data from 546 patients in methadone maintenance treatment. In this sample, women often started opiate use because of an already consuming partner, got addicted at an earlier age and attended the first therapy after a shorter duration of addiction. On the other side, men had more legal problems. There was no worse course found for women. Luthar et al. [14] compared 106 women and 96 men with opiate dependence. Women had more internalising, men more externalising disorders in childhood; also, women had more psychiatric problems, men more legal problems. No results on the course of dependence were reported.

In summary, there is only a limited number of studies regarding a gender-specific course of opiate addiction. In addition, all cited studies were carried out in the USA. It could be questioned whether the investigated samples, e.g. patients in maintenance treatment, are representative for opiate addicts in general. Data are missing whether the course of other problems besides consumption and physical problems is worse in women than men. Up to now, there were only comparisons of current states. There are no studies investigating whether a telescoping effect can be differentially observed under the conditions of different health-care systems or different legal orders, e.g. regarding the possession and consumption of drugs.

In this multicenter, European wide study we investigated gender differences in the course of opiate addiction. As evidence for a telescoping effect women should start regular opiate consumption later than men and should have a more severe dependence than men with the same duration of drug use. Apart from the physical consequences, we compared legal, financial, and social consequences between genders. In addition, the influence of other variables on the course of addiction was analysed, especially treatment experience, and country of recruitment.

Methods

Subjects and instruments

The study was part of the TREAT Project [21] which was conducted in six large urban European cities. Major aims of the study were a systematic and comparative description of the health-care system for drug (predominantly opiate) addicts in different European cities as well as of the clinical course of drug addicts over 18 months after starting a new treatment episode in the respective cities. The participating cities were chosen according to the type of national treatment system based on the typology of Klingemann and Hunt [11]: Athens (Greece) and Padua (Italy), as examples of systems where the tradition of treating alcohol dependence largely shaped treatment; London (Great Britain) and Zurich (Switzerland) as experimental systems; Stockholm (Sweden), representing an approach mostly based on the paradigms of drug prohibition and abstinence and Essen (Germany), as an approach primarily determined by cost-efficient pragmatism.

In each of the six cities (Athens, Essen, London, Padua, Stockholm, and Zürich), 100 opiate-dependent patients were investigated by a structured interview. Recruitment took place at various institutions of the local health-care systems for drug addicts, such as maintenance clinics, detoxification wards, and drug counselling services. To investigate a representative sample, the number of patients recruited at each institution was determined according to the relative importance of the respective institution within the local health-care system for drug addicts based on an evaluation of local experts. Subjects presenting at the respective institutions were consecutively admitted to the study.

Inclusion criteria were opiate addiction according to ICD-10 (alone or in combination with other substance related disorders), at least 18 years of age, and starting an episode of counselling or treatment in the recruiting institution. There were no exclusion criteria devised. The European addiction severity index (EuropASI; [7]) was completed in all interviews. Comorbid psychiatric disorders were recorded with the composite international diagnostic interview [24]. An interview lasted about 2 h. The patients received €20 (in cash or vouchers) for each interview.

The study has been reviewed by the ethics committee of the University of Duisburg–Essen and has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. All participating persons gave their informed consent prior to their inclusion in the study.

Statistical analysis

Two different and separated approaches were used for data analysis. First, women and men were matched regarding age and recruiting city. This reduced sample was tested by means of *t* test and χ^2 test for gender-specific differences regarding age of onset of regular heroin use and the severity of dependence.

Second, multiple linear and logistic regressions were calculated. Predictors for the severity of dependence were (1) duration of regular opiate consumption, (2) gender, (3) use of therapy in the last 6 months, (4) employment status, (5) living in a protective environment (e.g. hospital or prison), (6) recruiting cities as dummy variables, and (7) interaction term of gender and duration of consumption. The last predictor was the indicator for a telescoping effect. The severity of dependence was operationalised by the nine composite scores of the EuropASI and by binary criteria for the logistic regressions, such as employment status, living arrangement, HCV infection or a history of arrest; for an overview (see Table 1). Regressions were calculated according to the centring defaults by Kraemer and Blasey [13]. Backwards elimination in three steps with the interaction term as the last predictor being added was used.

To assess the telescoping effect, only patients with a regular consumption of up to 6 years were included in the regressions. Thereby, the risk of a masking of a telescoping effect by the chronicity of opiate addiction should be reduced. If an effect still could not be found, the years of consumption for inclusion shall be lessened.

Results

Sample

After the exclusion of a patient investigated two times at different institutions, sample size was $N = 599$. Out of them, 154 (25.7%) were female. Mean age was 33.0 years ($SD = 8.0$), mean age at onset of regular heroin use was 20.9 ($SD = 5.7$), and mean duration of regular opiate consumption was 11.9 years ($SD = 7.3$). Regarding living conditions, 59.4% of the patients reported that they were unmarried, 25.5% were living alone, 21% with their parents. Currently unemployed were 72.8% of the sample.

Matched sample

One hundred and forty men and women, respectively, could be matched regarding age and recruitment centre. Age at beginning of regular consumption [men 20.55 ($SD = 5.1$), women 21.4 ($SD = 6.4$)] did not differ significantly between both N groups [$t(242.1) = -1.16$; $p = 0.25$]. The composite score for medical problems was higher in women [0.4 ($SD = 0.4$)] than in men [0.2 ($SD = 0.3$); $t(277) = -3.01$; $p < 0.01$], but all other composite scores did not show significant differences. Men had more legal problems regarding incarcerations, were more often living alone or were homeless [$\chi^2(8) = 32.9$; $p < 0.001$]. The number of detoxification treatments was not different between men and women, but more men had

Table 1 Overview of the regression analyses

Predictors	Criterion:degree of dependence	
	Linear regression	Logistic regression
Duration of dependence (in years)	CS economic ^a	History of arrest
Gender	CS drugs	Stable living arrangement
Therapies in last 6 months	CS alcohol	
Inpatient detoxification	CS medical	Employment status
Inpatient long-term treatment	CS legal	
Outpatient substitution	CS psychiatric	HCV infection
Heroin consumption last 30 days ^b	CS family	
Employment status ^c	CS social	
Protective environment last 30 days	CS work	
Interaction gender \times duration of dependence	Satisfaction	
Recruitment centre (5 dummy variables)		

Predictors were identical in each regression except where indicated

^a CS composite score from EuropASI; range 0–1

^b Variable was not used as predictor in regression of CS drugs because it is part of it

^c Variable was not used in regression of CS economic and CS work satisfaction

been in long-term rehabilitation treatment than women (51.9 vs. 17.5%; $\chi^2(9) = 23.73$; $p < 0.01$). The results are shown in Table 2.

Sample in the regressions

A sample of $n = 130$ patients (90 men, 69.2%) was included, who had consumed opiates for up to 6 years. Men had significantly higher values than women regarding the number of months spent in jail [$t(96.25) = 2.01$; $p < 0.05$] and the current frequency of drinking alcohol [$t(119.88) = 2.26$; $p < 0.05$]. There were no further significant differences between groups regarding living conditions and drug history.

Multiple regressions

In the multiple logistic regressions, no significant effect was found for the interaction term of gender and duration of consumption. No effect for gender was found either. The duration of consumption was a significant predictor for the status of HCV infection. Similar results were found for the regression of the composite scores. The telescoping effect could not be proved. Among the variables of treatment experience, number of detoxification treatment was a significant predictor for the composite score “Drug”, whereas long-term rehabilitation treatment was a significant predictor for the composite scores “economic” and “legal” problems. Table 3 shows the results of these regressions.

Table 2 Differences between men and women in matched sample ($n = 280$)

Variable	Men ($n = 140$)	Women ($n = 140$)
Age (SD)	32.2 (7.4)	32.1 (7.5)
Duration of consumption (SD)	11.6 (6.9)	10.5 (7.5)
Age beginning regular heroin consumption	20.6 (5.1)	21.4 (6.4)
Age first injection	21.5 (5.4)	21.1 (5.5)
Years of education*	10.0 (1.9)	10.4 (2.7)
No regular work (%)	71.9	80.0
No school leaving qualification (%)	14.3	7.8
No completed vocational training (%)	50.0	41.4
Driving licence (%)	31.2	35.7
At least one detoxification treatment (drugs) (%)	64.9	53.0
At least one long-term inpatient treatment (drugs) (%)**	51.9	17.5
(ever in) Maintenance treatment (%)	53.1	61.2
Patient on parole (%)**	33.3	7.3
Months in arrest (total)***	20.1 (34.4)	4.7 (13.1)
HIV positive (%)	2.3	5.3
HCV positive (%)	61.5	53.0
Marital status		
Unmarried (%)	64.6	48.9
Married (%)	6.2	13.0
Remarried (%)	0.8	0.8
Divorced (%)	13.8	22.1
Separated (%)	13.1	13.0
Widowed (%)	1.5	2.3
Missing (%)	6.8	3.6
EuropASI composite scores		
CS medical**	0.2 (0.3)	0.4 (0.4)
CS economic	0.8 (0.4)	0.8 (0.3)
CS alcohol	0.1 (0.2)	0.1 (0.2)
CS drugs	0.3 (0.1)	0.3 (0.1)
CS legal status	0.3 (0.3)	0.2 (0.3)
CS psychiatric status	0.2 (0.2)	0.3 (0.2)
CS family	0.2 (0.2)	0.2 (0.2)
CS social	0.1 (0.2)	0.2 (0.2)
CS work satisfaction	0.2 (0.3)	0.3 (0.3)

Women and men were matched according to the age and recruitment centre

CS composite score

* $p < 0.05$ ** $p < 0.01$

*** $p < 0.001$ (two-tailed t test or χ^2 test, $\alpha = 0.05$)

Table 3 Results of multiple regression in the sample of patients with 6 years of consumption ($n = 130$)

Criterion	Significant predictors	$R^2_{\text{Nagelkerkes}}/R^2_{\text{corr}}$
Multiple logistic regressions		
History of arrest	Duration of dependence, Stockholm (RC)	0.137
Living arrangement	No. of homeless patients too small	–
Employment status	Padua (RC), Stockholm (RC), long-term treatment, protective environment	0.298
HCV infection	Duration of dependence, London (RC), Stockholm (RC)	0.260
Multiple linear regression		
CS Drugs	Athens (RC), Essen (RC), London (RC), Stockholm (RC), detoxification, employment status, protective environment	0.440
CS alcohol	Essen (RC), London (RC)	0.03
CS economic	Athens (RC), Essen (RC), London (RC), Stockholm (RC), long-term treatment, Heroin 30 days	0.217
CS work satisfaction	Essen (RC), Padua (RC), Heroin 30 days	0.053
CS legal	Essen (RC), Stockholm (RC), long-term treatment, Heroin 30 days	0.266
CS medical	London (RC), Heroin 30 days, protective environment	0.092
CS psychiatric	Athens (RC), London (RC), Stockholm (RC), substitution	0.051
CS family	Gender, duration of dependence, Substitution	0.056
CS social	Padua (RC), employment status, protective environment	0.033

RC recruitment centre

When the inclusion criterion was reduced to 4 or to 3 years of consumption, the interaction of gender and duration of consumption was a significant predictor for the composite scores for economic, legal, alcohol, family, and social problems. Regarding the regression of the first three composite scores (economic, legal, and alcohol), a telescoping effect was found for men, i.e. men had a higher problem severity given the same duration of regular opiate use than women. For the last two composite scores (family and social), women had a faster progression. The results are shown in Table 4. A significant main effect for gender was only found for the composite score economic problems. Women had more economic problems than men. The composite scores economic, alcohol, and legal were significantly predicted by the duration of regular consumption.

Finally, the regressions were repeated for a sample of patients with up to 15 years of consumption ($n = 397$, 26.2% women). A telescoping effect was only found within the regression of the status of HCV infection. Women had a significantly higher probability to get infected when consuming longer.

It is noteworthy that in all analyses (duration of regular opiate use up to 4 years/up to 6 years/up to 15 years), the recruitment centres were significant predictors, especially

in the regressions of the composite scores “drugs” and “legal” problems.

Discussion

In this investigation, the telescoping effect could not be proven in a large sample of patients with long-term opiate addiction. In a comparison of female and male patients matched for age and study centre, age of onset of regular heroin use was similar in women and men. Given the similar duration of regular heroin use of about 11 years, current severity of dependence measured with the problem scores of the EuropASI was not different. Among the few differences was a higher burden with legal problems for men. There was no difference in the burden of psychiatric problems between female and male patients (related data from research in alcohol addiction [16]). In an additional analysis with a variation of the length of opiate addiction, a gender-specific course of dependence could only be proved up to a regular consumption duration of 4 years. They appeared as a faster progression of economic, legal, and alcohol problems in men, and of family and social problems in women. After a longer duration of consumption

Table 4 Results of regression analyses for different inclusion criteria

Duration of dependence (years)	<i>n</i>	Women (%)	Telescoping effect	Main effect Gender ^b	Main effect duration of dependence ^b
6	130	30.8	–		
5	107	32.7	–		
4	87	32.2	CS fam (F > M)*	–	–
			CS soc (F > M)*	–	–
			CS eco (M > F)*	F > M	x
			CS alcohol (M > F)*	–	x
			CS legal (M > F)*	–	–
3	63	41.3	CS fam (F > M)**	–	–
			CS soc (F > M)**	–	–
			CS eco (M > F)*	F > M	x
			CS legal (M > F)**	–	x
2	43	39.5	–		
1	15	33.3	No computation		

^a '>' stands for faster progression; * $p < 0.05$, ** $p < 0.01$

^b Main effects for gender and duration of dependence are only shown for those variables with a telescoping effect

(15 years), there was only a telescoping effect found for the status of HCV infection in women. This effect can be due to a higher risk of infection for women because of prostitution or attachment to a drug-addicted partner [19]. In the sample with patients consuming opiates for up to 4 years, women underwent more often detoxification treatment, whereas in the matched sample with more years of consumption, men underwent more often long-term rehabilitation treatment.

It is noticeable that mainly the recruitment centres are significant predictors for the degree of dependence in the patients, and are of more importance than gender. Therapies have less influence on the criteria, although there are effects of detoxification on consumption or of long-term rehabilitation treatment on economic or legal problems. The duration of consumption only had influence on HCV infection or history of arrest. A possible explanation for this finding is that these criteria remain positive, once they are fulfilled and, thus, must have a higher probability with increasing age.

In summary, the telescoping effect in opiate dependence is not comparable to the effect found for alcohol dependence. There is no general gender-specific effect, but domain-specific effects with a partly higher problem intensity for women, partly for men. At best, the telescoping effect could be observed in the first 4 years of dependence. Then, opiate dependence tends to a chronification, and shows only individual variations that impeded significant predictions by gender or duration of consumption.

It has to be discussed why there is only limited evidence for a telescoping effect in opiate addiction compared with the stronger evidence in alcohol addiction. First, the

telescoping effect in alcohol addiction is partly explained as a consequence of gender-specific metabolism of alcohol rendering women to higher risk of physical damage due to alcohol and its toxic metabolites [4]. For heroin, a gender-specific toxicity cannot be assumed in a similar way [3]. Second, it has to be assumed that the development of opiate addiction including its harmful consequences is faster than the development of alcohol addiction. Not the least due to its state as illegal substance sold for high prices on a black market and often being associated with illegal activities as well, the harmful consequences are often already manifested in the first years of heroin addiction.

The influence of other factors on the course of dependence such as center differences in this European wide investigation seem at least on par with gender effects. However, it is not clear which factors are responsible for differences in the course and severity of opiate addiction between countries. Possible variables are national differences in the availability costs of drugs [15], in the extent and thresholds of treatment measures [5, 6, 12], or in the laws regarding drug-related criminal behaviour.

Limitations

The age at first treatment is not asked for in the Europ-ASI. Therefore, gender difference regarding the duration of addiction until the first treatment could not be investigated. This could be adjusted using the number of therapies as a covariate or as predictor in the regressions. Second, the study was carried as a cross-sectional study in patients with various duration of opiate addiction.

However, there is no point for systematic gender-specific errors of the results due to this design. Third, the influence of therapies on the presumably fluctuating severity of dependence could have been investigated more intense in a prospective design. Fourth, in accordance with the aims of the TREAT study, our sample is limited to drug addicts starting a new treatment episode in the health-care system for drug addicts. Our sample is, therefore, not representative for drug addicts in general, including addicts currently not in treatment. However, in the long-term course of opiate addiction patients go in and out of treatment with only a small minority with no treatment experience [22]. Owing to choosing recruitment sites offering different kinds of counselling and treatment, our sample is more representative than samples in previous studies that are limited to a specific treatment, e.g. methadone maintenance treatment.

The high influence of recruitment centres as predictors can be the influence of systematic recruiting errors, although inclusion criteria were simple and clearly determined. The method of backwards elimination in multiple regressions is often criticised for making too optimistic estimations which are only valid for the analysed sample [18]. However, the aim of this study was not to analyse relations between other variables such as treatment experience and the degree of dependence. We wanted to show how much influence a possible telescoping effect has in addition to other variables, so that backwards elimination led to an easier estimation of this effect in contrast to others.

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