Craving for benzodiazepines : the development of the benzodiazepine craving questionnaire

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Summary

CRAVING FOR BENZODIAZEPINES
The development of the Benzodiazepine Craving Questionnaire

This thesis describes the development and initial validation of the Benzodiazepine Craving Questionnaire, a Rasch-homogeneous self-report questionnaire to assess craving for benzodiazepines. This questionnaire was developed as part of the Benzoredux project, which was designed to evaluate a stepped-care approach to reduce long-term benzodiazepine use in general practice.

In **chapter 1** some aspects of (long-term) benzodiazepine use are discussed, such as its definition and prevalence, and drawbacks of this use, e.g. dependence. Subsequently, we address the role of craving in dependence on addictive substances, and discuss some models of craving and recent developments in craving research. We find that benzodiazepine craving research is scarce and that a good benzodiazepine craving questionnaire is lacking. These observations are the starting point of the development of the Benzodiazepine Craving Questionnaire and of this thesis.

In **chapter 2** we describe the development and initial validation of a newly constructed self-report questionnaire assessing craving for benzodiazepines, the Benzodiazepine Craving Questionnaire (BCQ). The BCQ was administered to a sample of 113 long-term and 80 former long-term general practice benzodiazepine users participating in the Benzoredux project. The BCQ met the requirements for Rasch homogeneity, i.e. self-reported benzodiazepine craving as assessed by this questionnaire can be regarded as a unidimensional construct. Reliability, as indicated by the subject and item discriminability, was good. Construct validity was modest: correlations between BCQ sum scores and other variables (dependence, personality, and psychopathology) were low. Discriminative validity was satisfactory. The first signs of craving were represented by the acknowledgement of expectations of positive outcome and of relief of withdrawal or negative affect, whereas desire, lack of control over use and direct intention to use were only found in cases of high craving. The BCQ was found to be a reliable and psychometrically sound self-report instrument to assess benzodiazepine craving in a general practice population of (former) long-term benzodiazepine users.

Chapter 3 aims to describe characteristics of patients reporting craving for benzodiazepines and to search for associations between benzodiazepine craving and other clinical variables in a population of general practice patients who had made an attempt to discontinue their long-term benzodiazepine use. Patients reporting craving for benzodiazepines on the BCQ differed significantly from patients not reporting craving on aspects of benzodiazepine dependence severity, psychological well-being, aspects of health-related quality of life,

aspects of a negative mood state (depression and anger), and certain personality traits (somatisation and negativism). Furthermore, in a multivariate analysis, controlling for current use status, depression and somatisation were positively associated with benzodiazepine craving. However, only the contribution of depression to craving was statistically significant for the total group of (former) benzodiazepine users (p = .002). These results call for further research with respect to the relationship between personality and benzodiazepine craving.

Since craving for different substances of abuse has been described to fluctuate over time, it is important that craving questionnaires are sensitive to changes over time. Therefore, in **chapter 4** we have aimed to assess benzodiazepine craving longitudinally and have described its course by means of the BCQ. A subset of 117 (former) long-term benzodiazepine users received four repeated measurements of the BCQ, taken over a 21-month follow-up period. Results indicated that benzodiazepine craving severity decreased over time. Patients still using benzodiazepines experienced significantly more severe craving than patients who had quit their use after either a minimal intervention (letter from their general practitioner with the advice to quit their use) or after a subsequent randomised controlled trial (tapering off programme with or without additional group cognitive-behavioural therapy). The method of discontinuation did not influence the experienced craving severity over time. However, patients who had received the additional tapering off programme, on average, reported significantly more severe craving than patients who had only received a letter from their general practitioner as an incentive to quit. It was concluded that, although benzodiazepine craving was prevalent among (former) long-term benzodiazepine users in our study population during and after discontinuation, it decreased over time to minimal proportions. Nevertheless, the BCQ proved to be an instrument capable of monitoring and quantifying craving for benzodiazepines longitudinally and it was sensitive enough to discriminate between different subgroups. The BCQ sum scores may give direction to the advisable treatment intensity, in terms of type of interference by the general practitioner, when a patient is trying to abstain from benzodiazepines.

Chapter 5 addresses the scope of the craving definition (broad versus narrow). We compared a broad conceptualisation of benzodiazepine craving, as represented by the BCQ, with a narrow one, as represented by the sum score of three one-item Likert-type scales assessing the frequency, global intensity and peak intensity of the desire for benzodiazepines when not using (the Benzodiazepine Desire Scale, BDS). In a factor analysis the BCQ loaded on a factor representing negative affect, while the BDS loaded on a dependence factor. Apparently, low craving, as measured with the BCQ, is associated with negative affect and reflects the anticipation of positive outcome of benzodiazepine use and of relief from negative affect or withdrawal. The low BCQ sum scores in our study population and the selected time frame of the craving measurement (current experience versus over the past week) were the most likely explanations for our findings. Both

conceptualisations of benzodiazepine craving contribute to our understanding of the potential significance and meaning of craving in benzodiazepine use.

Chapter 6 presents a Cox-regression analysis used to identify independent predictors of relapse after benzodiazepine discontinuation, with time to relapse as the dependent variable. Potential predictors included benzodiazepine (usage) characteristics, psychopathological symptoms, personality traits and characteristics of benzodiazepine dependence, including craving as measured with the BCQ. The BCQ sum score had no predictive value with respect to relapse after a minimal intervention (letter from the general practitioner). However, independent predictors of relapse during a 15-month follow-up period after a tapering off programme included higher craving sum scores on the BCQ, higher age, public health insurance, and higher 'lack of compliance' with the therapeutic benzodiazepine regimen. These results should guide relapse prevention programmes by including treatment elements with a focus on (coping with) craving experiences.

Chapter 7 mainly considers points of discussion that have not been addressed in the previous chapters. Furthermore, the major conclusions are presented along with recommendations for further research and some clinical implications.

First of all, we examine the generalisability of our results further and conclude that generalisability was probably reduced due to the large amount of patients who refused to take part in the Benzoredux study. Mainly low-dose benzodiazepine users took part in the study. Benzodiazepine dependence might have played a role here. Our findings probably represent daily clinical practice, as particularly those patients will take part in a discontinuation trial who are prepared to try to discontinue their benzodiazepine taking. Therefore the present study should be repeated in a less selective sample.

With regard to the development of the BCQ, the pros and cons of the use of the Rasch scaling model as compared with 'classical test theory' are addressed. The 'item response theory' or 'latent trait theory' on which the Rasch scaling model is based, justifies the use of the BCQ sum score as a measure for the underlying unidimensional construct of craving. The BCQ sum scores were low on average, which indicates that craving did not seem to be a big issue in our study population.

Comparing our study results with (neuro)biological findings from craving research into other substances of abuse, we have found some similarities with 'relief craving', as described in the 'three-pathway psychobiological model of craving for alcohol'.[1] However, benzodiazepine craving research in this field of expertise is lacking.

In our study population, expectations of positive effects of benzodiazepine use constitute the first signs of benzodiazepine craving. This makes our study results interpretable from the perspective of different cognitive theories on craving, e.g. the cognitive social learning theory. Treatment strategies should take these explicit drug expectancies into account.

BCQ items indicative of more severe craving for benzodiazepines, referring to the desire to

use benzodiazepines, the intention to use, and lack of control over use, were hardly confirmed in our study population. Further research in other, high-dose and high-dependence benzodiazepine-using populations should reveal whether craving in these groups covers the entire spectrum of BCQ items. Up till now it is unclear whether different groups of users have different craving profiles.

In addition to repeating the present study in different populations, the usefulness of the BCQ can be further improved by means of Latent Trait Standardisation on the basis of a normative population of general practice benzodiazepine users. It would make raw BCQ scores clinically interpretable in relation to the normative population. This would increase the usefulness of the BCQ in benzodiazepine reduction programmes in general practice.

Reference

1 Verheul R, Van den Brink W, Geerlings P. A three-pathway psychobiological model of craving for alcohol. Alcohol & Alcoholism 1999;34(2):197-222