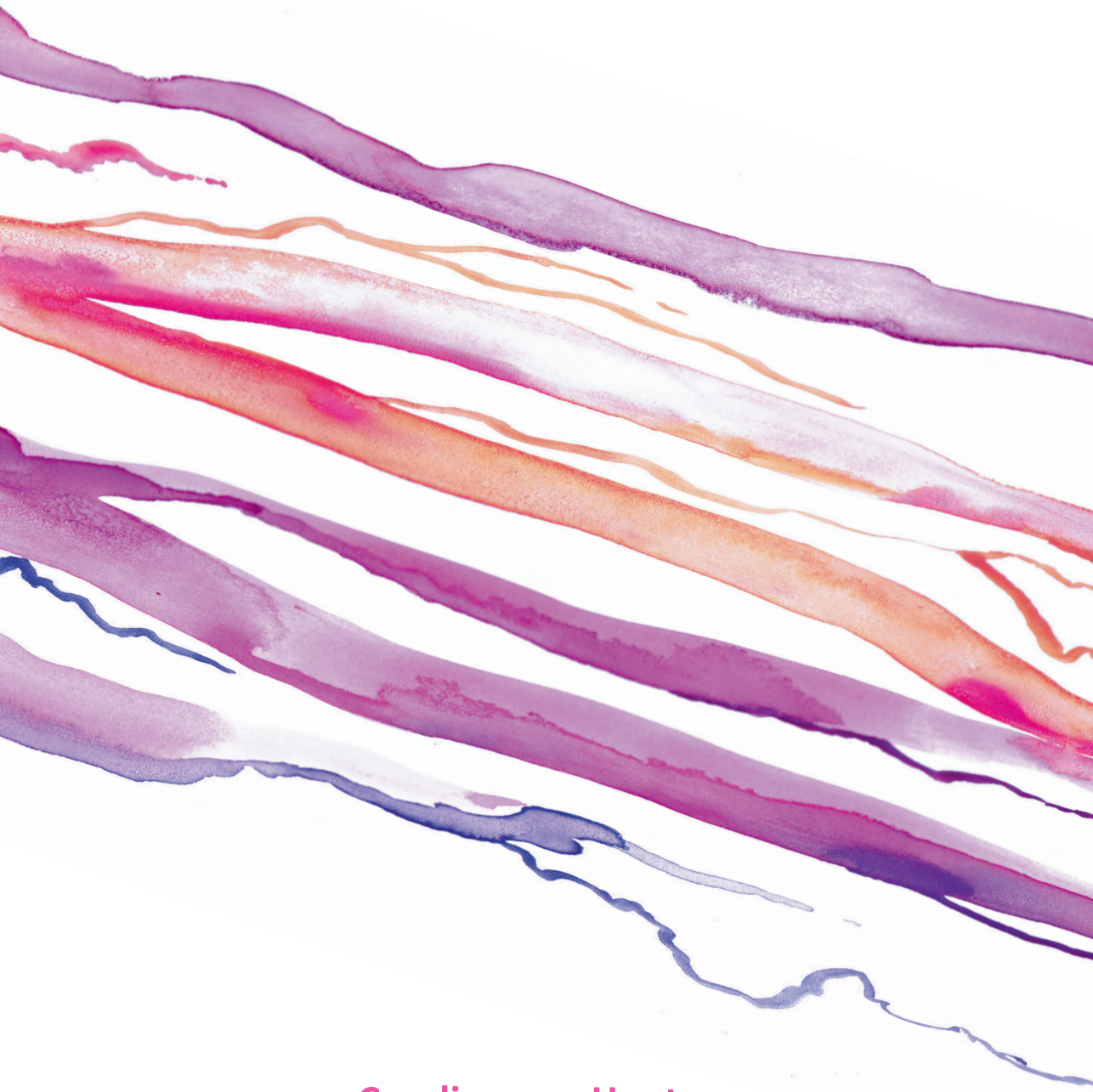
ANXIETY, FAINTING AND GAGGING IN DENTISTRY

SEPARATE OR OVERLAPPING CONSTRUCTS?



Caroline van Houtem

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COLOFON

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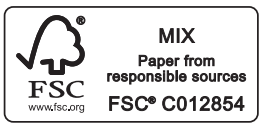

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Promotiecommissie

Promotor:	Prof. dr. A. de Jongh	Universiteit van Amsterdam
Copromotor:	Dr. A.J. van Wijk	Universiteit van Amsterdam
Overige leden:	Prof. dr. M.A.J. Eijkman	Universiteit van Amsterdam
	Prof. dr. M. van der Gaag	Vrije Universiteit Amsterdam
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	Prof. dr. B.G. Loos	Universiteit van Amsterdam
	Dr. C.M. Visscher	Universiteit van Amsterdam

Faculteit der Tandheelkunde

Paranimfen: Dr. J.H. Vermaire
Drs. J. den Engelsen

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CHAPTER 1

General introduction

The overarching topic of this thesis is dental anxiety and its severe form, dental phobia. These phenotypes, and the emotions attached with these, can complicate dental treatment, not only for the patient, but also for the oral health professional. For most people it is obvious that dentally anxious and dentally phobic patients undergo treatment with feelings of inconvenience and discomfort, if treatment is not avoided at all. To treat these patients so called "special dental care clinics" were founded (Aartman et al., 1997). In such clinics not only patients with high levels of dental anxiety or dental phobia are treated, but also patients with, for example, severe gagging problems and fainting problems.

In the present dissertation, the focus is on these three patient categories (i.e., those with severe levels of dental anxiety or dental phobia, those who severely gag during dental treatment, and those with fainting problems related to dental treatment), who visit special dental care clinics. The general purpose of this dissertation is to increase the knowledge about dental anxiety, dental phobia, gagging and fainting during dental treatment. The main aim is to find an answer to the question as to whether or not these conditions are inter-related, or should be considered as separate entities. In the remainder of this chapter a description of relevant background topics is given, and an outline of the studies that are part of the dissertation. Firstly, the relevant background regarding dental anxiety and dental phobia is presented. This is followed by a summary of the literature pertaining to the alleged etiology of anxiety and anxiety disorders, including dental anxiety and dental phobia. Next, a background is provided regarding fainting and gagging related to dental treatment. Finally, a short overview is presented of heritability studies about fear and phobias, including the scarcely available literature concerning the heritability of dental fear. For all the topics mentioned above, the gaps in the literature were assessed, which have served as the basis for the studies in this thesis.

Dental fear, dental anxiety and dental phobia

Fear is a normal response to a genuine danger (American Psychiatric Association, 2013) and that is why dental fear is considered to be a normal emotional reaction to a perceived threat in the dental setting (Klingberg & Broberg, 2007). Dental anxiety is defined as a more general state of anticipatory concern related to dental treatment. Dental phobia is a severe (pathological) form of dental fear and dental anxiety, and is defined as a disproportional fear of (invasive) dental procedures (American Psychiatric Association, 2000). According to the Diagnostic and Statistical Manual of Mental Disorders (DSM–5; APA 2013, pp 298) dental phobia is classified as a specific phobia, an anxiety disorder that is characterized by: a) a marked and disproportional fear within an environmental or situational context to the presence or anticipation of a specific object or situation; b) exposure to the phobic

stimulus provokes an immediate anxiety response, which may take the form of a situationally bound panic attack; c) the person recognizes that the fear is out of proportion; d) the phobic situation(s) is avoided or else is endured with intense anxiety or distress; e) the avoidance, anxious anticipation or distress in the feared situation(s) interferes significantly with the person's normal routine, occupational (or academic) functioning, or social activities or relationships, or there is marked distress about having the phobia. Furthermore, the symptoms for all ages must have a duration of at least 6 months.

Prevalence of dental anxiety and dental phobia

It is assumed that dental fear, dental anxiety and dental phobia may develop from childhood (Locker, et al., 1999; Öst, 1987) to adulthood (Oosterink et al., 2009; Locker et al., 1999). A review article analyzing the literature on dental anxiety of the past 50 years found no clear answer to the question as to whether the prevalence of dental anxiety has increased or decreased over the last decades (Smith & Heaton, 2003). Yet, it has been found that about 25%-40% of the adult population in Western societies, including The Netherlands, report moderate dental anxiety (Halonen et al., 2014; Singer et al., 2012; Oosterink et al., 2009) and 5%-18% of the population, suffers from high levels of dental anxiety, depending on the sampling methods, specific measures and cut-off points used (Hill et al., 2013; Humphris & King, 2011; Armfield, 2010; Nicolas et al.; 2007; Schuller et al., 2003; Locker, 2003; Hakeberg et al., 1992), whereas 2%-4% suffers from dental phobia (Oosterink et al., 2009; Stinson et al., 2007; Fredrikson et al., 1996).

Association of dental anxiety with socio-economic background variables

On average, women report higher levels of dental fear and anxiety than men (e.g., Humphris & King, 2011; Oosterink et al., 2009; Schuller et al., 2003; Stouthard & Hoogstraten, 1990), but women do not fulfill the screening criteria for dental phobia more frequently than men (Oosterink et al., 2009; Fredrikson et al., 1996). With respect to level of education, contradictory findings are reported in several studies. Some studies indicated that individuals with a low level of education are more likely to report a high level of dental anxiety compared to those with a higher level of education (e.g., Erten et al., 2006), but other studies failed to find such an association (Vassend, 1993; Stouthard & Hoogstraten, 1990). Furthermore, a high level of dental anxiety and dental phobia has been found to be associated with irregular dental care or avoidance of dental care (Hill et al., 2013; Armfield, 2013; Armfield et al., 2007), a deteriorating oral health (Schuller et al., 2003; Stouthard & Hoogstraten,

1990), a lower health related and generic quality of life (Vermaire et al., *in press*; Vermaire et al., 2008; Mehrstedt et al., 2007) and a negative impact on social life (Cohen et al., 2000). Thus, it is clear that high levels of anxiety or dental phobia can negatively affect peoples' wellbeing.

The etiology and maintenance of anxiety in general, dental anxiety and dental phobia

Most people are familiar with the fact that distressing events tend to be well remembered and leave behind lasting and vivid memories (e.g., McIntyre & Roozendaal, 2007; McGaugh, 2004). Enhanced memory for disturbing events can be extremely functional, because this mechanism helps us to remember threatening situations (McGaugh, 2004) and gives us guidance for future actions. However, distressing experiences may also lead to highly aversive memories, which may contribute to the development and maintenance of anxiety and related conditions (Kindt & Soeter, 2011; De Quervain et al., 2009; Pratt et al., 2004). Reactivation and retrieval of these disturbing memories can lead to a physical fear response (Cuthbert et al., 2003), such as an increased heart rate (Leutgeb et al., 2011).

Also for the development of dental anxiety and dental phobia the negative affect associated with the experience of a disturbing (dental) event appears to be an important conditioning factor which could lead to the formation of aversive memories (Humphris & King, 2011; Oosterink et al., 2009; Locker et al., 1999; Moore et al., 1991). A limitation of previous studies regarding aversive memories and dental anxiety is that the self-reported content and characteristics (disturbance, emotionality and vividness) of these memories were not examined or at least not reported. Empirical studies in other domains of anxiety disorders found that not just the content, but also the emotional characteristics of those memories are associated with symptom severity (e.g., Arntz et al., 2005; Berntsen et al., 2003). Another limitation is that we do not yet know whether, and in what way, the memories of these past disturbing events play a role in the maintenance of dental trait anxiety, and whether the characteristics of these memories are associated with current anxiety levels. Lastly, it has not investigated as yet whether individuals who are highly anxious about the dental situation, when confronted with their fear eliciting stimuli (for instance, an invasive dental treatment), store more disturbing memories of this event compared to low anxious individuals, which would not only explain the severity of individuals' fear response, but also the difficulties dentists sometimes face when trying to treat them. Although these results have been found in laboratory studies, translational research in a relevant clinical setting is lacking and greatly needed.

The heterogeneous nature of dental fear

Dental fear may not be considered as a homogeneous phenomenon, but as a collective term for fear of one or more objects and situations present in the dental setting (e.g., Oosterink et al., 2008; De Jongh et al., 1998). Oosterink identified 67 objects or situations within the dental setting that were potentially fear provoking (Oosterink et al., 2008). The question is whether this broad collection of objects or situations can be subdivided in distinct typologies that may relate to different treatment strategies. Oosterink and colleagues performed an exploratory factor analysis on the set of 67 stimuli using a sample of a 1,000 individuals. They identified a two-factor solution, with a first factor being an 'invasive treatment-related stimuli factor', and a second being a 'non-invasive-treatment related factor'. However, close inspection of the results suggests that the two factors were very general in nature, with only a modest proportion of explained variance (51.4%). In addition, a number of items showed low factor loadings and/or low communalities. This suggests that a more complex factor structure may be underlying the various situations and objects that make the dental setting fear provoking for many individuals. Building on the work of Oosterink et al. (2008), Wong and colleagues (Wong et al., 2015) conducted both an exploratory (EFA) and a confirmatory factor analyses (CFA) on 73 items, thereby covering the same 67 potentially fear-eliciting stimuli as well as six additional items. Their EFA revealed a seven-factor solution (dental check-up, perceived lack of control, clinic environment, injection, scale and drill, surgery and empathy) that explained 71.3% of the total variance. However, in this study the sample was relatively heterogeneous and the number of individuals included in the EFA and the CFA was low relative to the number of items, which potentially reduces the generalizability of the results. Therefore, replicating the analysis using a larger and heterogeneous sample is likely to provide better insight in the distinct typologies underlying the construct of dental fear. This may be important for research, for the proper assessment of varying subtypes of fears, and for the development of appropriate treatment strategies (De Jongh et al., 2011).

Fainting or dizziness during dental treatment

In the DSM-5 dental phobia is classified as a specific phobia of the Blood-Injection-Injury (B-I-I) subtype (APA, 2013), a phobia subtype that is characterized by a negative response to blood, needles, injuries and invasive medical procedures (APA, 2013). According to the DSM-IV-TR (APA, 2000) the unique characteristic of B-I-I phobia is that a part of the individuals suffering from this condition display a strong vasovagal response following exposure to a phobic stimulus, which induces feelings of dizziness and an increased likelihood of vasovagal fainting (Page, 1994; Öst et al., 1984). This response is opposite to the normal cardiac re-

sponse observed in individuals with any other specific phobia, who show only an increase in heart rate, without the subsequent feelings of dizziness or fainting (e.g., Elsesser et al., 2006). Despite the fact that certain types of dental treatment can be considered as an invasive medical treatment (for instance extractions or placing dental implants), based upon clinical experience it is doubtful whether many dental phobics suffer from such a typical vasovagal fainting response (e.g., Leutgeb et al., 2011) as was suggested by the current classification of dental phobia within DSM-IV-TR (i.e., "Specific Phobias of the Blood-Injection-Injury Type, may have detrimental effects on dental and physical health, because the individual may avoid obtaining necessary medical care", page 446, APA, 2000)". In other words, we found it of importance to investigate whether the current classification of dental phobia, as part of the B-I-I cluster, could be justified.

Gagging during dental treatment

Gagging during dental treatment has often been found to severely interfere with dental treatment and may, therefore, be considered a barrier to successfully complete dental treatment. Using a MEDLINE-PubMed search with the themes: "gag reflex dentistry", "gag reflex dental", "gagging dentistry" or "gagging dental" we found that since 1953 only about 200 articles were published about gagging and dentistry. This shows that gagging during dental treatment is still a relatively unexplored area of dental research. A significant part of these studies appeared to include case reports (e.g., Packer et al., 2005), articles about patient management (e.g., Sari & Sari, 2010), and small case-control studies examining differences between gaggers on non-gaggers (e.g., Akarslan & Erten, 2010). However, basic information such as the prevalence rate of dental-treatment related gagging, and its possible socio-demographic correlates (i.e., gender, age, country of birth and level of education) of gagging in the general population proved to be greatly lacking. Also the question whether gagging during dental treatment would be associated with higher levels of dental anxiety and greater avoidance of dental care has not yet been resolved. To this end, until now only one study properly investigated dental attendance patterns in individuals with and without gagging problems showing no differences in visit frequency between gaggers and non-gaggers (Akarslan & Yildirim Biçer, 2013). Some studies showed that individuals who suffer from an excessive gag reflex experience the dental treatment as more fearful than those without severe gagging problems (Akarslan & Yildirim Biçer, 2013; Uziel et al., 2012; Winocur et al., 2011; Akarslan & Erten, 2010), although other studies failed to find such a difference (Van Linden van den Heuvell et al., 2008). Yet, it is also still unknown whether the increased levels of dental anxiety reported by those who suffer from gagging could best be explained by fear of certain stimuli specifically related to gagging (e.g., intraoral stimuli; Bassi et al., 2004),

typical dental objects and situations (e.g., pain, injections or the sound of the drill; Oosterink et al., 2009), or to an underlying general vulnerability factor.

Heritability of anxiety and phobia

Besides exposure to a distressing situation, there are two other pathways through which dental fears and dental anxiety (Oosterink et al., 2009) can be acquired (i.e., vicarious exposure and transmission of information and instruction; Rachman, 1977). But, these three pathways of fear alone do not always (e.g., King et al., 1998) or completely (e.g., Oosterink et al., 2008) explain why dental fears and phobias develop. Several authors claim that, in addition to Rachman's theory of fear acquisition (Rachman, 1977), a fourth pathway exists, namely a non-associative path (Poulton & Menzies, 2002). According to the non-associative theory of fear acquisition (Poulton & Menzies, 2002) some fears and specific phobias would be the result of innate fears shared by all humans. Besides, several authors state that some adults develop specific phobias because they either have an enhanced genetic liability to fear specific situations or have a deficit in the (probably genetically given) mechanisms to dispose themselves of fear responses (e.g., habituation or desensitization; Poulton & Menzies, 2002; Mineka & Öhman, 2002). Moreover, it has been suggested that for a number of specific phobias familial factors, which are partly genetic, influence the risk of developing specific phobias (Kendler et al., 1999).

Studies that tried to quantify the variance in a population due to genetic, shared environmental (i.e., family), and unique environmental (i.e., individual specific) influences for a certain trait or disorder are twin studies. These studies are a valuable source of information about the genetic basis of complex traits (Boomsma et al., 2002) by providing heritability estimates for a specific phenotype. In general, anxiety disorders have been found to be moderately heritable (Hettema et al., 2001). A meta-analyses of data from family and twin studies of several psychiatric disorders, including phobias, explored the role of genetic and environmental factors in the etiology of these conditions (Hettema et al., 2001). Strong support was found for a familial risk (i.e., a familial component to fears and phobias) for phobic disorders. In addition, phobias were found to be moderately heritable with an estimated heritability in the range from 20%-40%, depending on the type of phobia (Hettema et al., 2001). However, in this study the specific phobias were grouped together with the other main categories of phobias (e.g., agoraphobia), making it difficult to estimate the explained variance by genetic factors for a subtype of specific phobia *per se* (Hettema et al., 2001). Until now, only one study provides information about the estimated heritability of dental anxiety in an adult population (Vassend et al., 2011). The results showed that dental anxiety is moderately heritable. Since this study was conducted among a relatively small sample

of adult twins, replicating this study in a large sample of adult twins may give us additional information about the genetic liability to develop dental anxiety.

Conclusion and outline of this thesis

The literature presented above shows that the mechanisms underlying the etiology of dental anxiety and dental phobia are not completely understood. In addition, a limited amount of literature (showing contradictory results or gaps in knowledge) is available that pertains to dental treatment related fainting and gagging. Therefore, the purpose of this thesis is to increase the currently available knowledge about dental anxiety and dental phobia, as well as dental treatment related fainting and gagging. In order to achieve more insight in the aforementioned topics six studies are presented covering these topics. Yet, two important notes should be made here regarding the content of my dissertation. The first note concerns the original goal of my Ph.D. track. At the start, one of the main goals was to examine whether a deletion variant of one candidate gene, i.e., the ADRA2B-gene encoding the alpha-2B adrenergic receptor in de amygdala (e.g., De Quervain et al., 2007), would be more prevalent among individuals with high levels of dental anxiety than among those with average levels of dental anxiety. The main reason for this was the publication of a study, showing that individuals with the deletion variant compared to individuals without this deletion variant not only had a substantial enhancement of emotional memory for positive and negative pictures, but also increased re-experiencing symptoms of posttraumatic stress disorder (De Quervain et al., 2007). Our research group was interested in solving the question as to whether individuals with high anxiety levels would show enhanced emotional memory for events underlying their dental anxiety, and also whether they would be more likely to possess the deletion variant of the ADRA2B-gene than their low anxious counterparts. However, the inclusion of a sufficient large number of individuals with high levels of dental anxiety or dental phobia to conduct proper DNA-analyses during the period of my Ph.D. program turned out to be too time consuming because of the large drop out of participants. Consequently, my thesis does not contain data about the relation between ADRA2B-gene and the presence of enhanced emotional memory for experiences that are supposed to underlie their dental anxiety. Just before finishing my thesis, a large part of the collected DNA-samples collected over a period of 6 years could finally been analyzed. Unfortunately, the majority of the samples that were analyzed appeared to not contain enough DNA to perform further DNA-analysis.

The other important note relates to the fact that during my Ph.D. program we were given the ability to start a collaboration with the Netherlands Twin Register (Boomsma et al., 2006). Our aim was to collect data regarding dental anxiety, dental phobia, fainting and

gagging during dental treatment in order to get insight in the heritability estimates of these traits. However, again collection of sufficient data to conduct proper twin analyses appeared to be very time consuming and complicated. Therefore, it was not feasible to include any data about heritability estimates of dental anxiety, dental treatment related fainting and gagging in my PhD thesis.

The six studies included in my thesis are presented in the following order:

In *Chapter 2* an overview is provided of studies conducted in the field of heritability which were aimed to (1) gain insight into the background of heritability studies of specific phobias and corresponding fears; (2) develop a better understanding of the genetic liability to develop fears and phobias; and (3) to provide clues for future research regarding the heritability of specific phobias and corresponding fears.

In *Chapter 3* the results are described of an exploratory and a confirmatory factor analysis that were carried out among a large population-based sample. These were aimed to explore 1) the conceptual structure of dental fear and 2) to develop a descriptive framework for the classification of dental fear.

The results of a study that aimed to get more insight in the development and maintenance of dental trait anxiety are presented in *Chapter 4.* In that study the presence, content and characteristics of memories of events that initiated or exacerbated dental anxiety were assessed, as well as the relationships between current levels of dental trait anxiety and some key features of these memories. The study used a semi-structured interview and included dental phobics, subthreshold dental phobics, and normal controls.

Whereas Chapter 4 focusses on the etiology and maintenance of dental trait anxiety, *Chapter 5* focusses on dental state anxiety during dental treatment and the formation of memories of dental treatment. For the purpose of this study, a subsample of individuals investigated for the study presented in *Chapter 4* with either high or low levels of dental trait anxiety were exposed to an invasive dental treatment. Immediately after this treatment, and at two-week follow-up, the memory characteristics of both groups were assessed and compared. The possible association between dental state anxiety and characteristics of the memory was assessed and explained in the light of laboratory studies on memory formation and memory retrieval.

The aim of the study presented in *Chapter 6* was to determine the co-occurrence of dental phobia, typical dental (and B-I-I related) fears, vasovagal fainting, and avoidance of dental care in a large sample of individuals. Also the conceptual validity of dental phobia as part of the Blood-Injection-Injury (B-I-I) phobia subtype within DSM-IV-TR is discussed.

Research about dental-treatment related gagging describes large gaps in the existing knowledge on this phenomenon. Therefore, the purpose of the study presented in *Chapter 7* was to supplement the existing information about gagging during dental treatment. The

aims of the study were to derive a prevalence estimate of gagging during dental treatment in a large sample, to investigate some socio-demographic and psychological correlates of gagging, and the relationship between gagging and self-reported oral health and avoidance of dental care.

In *Chapter 8* a general discussion and summary are presented as well as practical and theoretical implications and suggestions for future studies.

This thesis is based upon four publications in peer reviewed journals and two research articles that are submitted for publication. The information in some of the publications or submissions shows overlap or is redundant. Therefore, all abstracts were removed and the text was uniformed as much as possible.

References

Aartman, I. H. A., De Jongh, A. & van der Meulen, M. J. (1997). Psychological characteristics of patients applying for treatment in a dental fear clinic. European Journal of Oral Sciences, 105: 384–388.

Akarslan, Z.Z. & Yildirim Biçer, A.Z. (2013). Influence of gag reflex on dental attendance, dental anxiety, self-reported temporomandibular disorders and prosthetic restorations. Journal of Oral Rehabilitation, 40: 932–939.

Akarslan, Z.Z. & Erten, H. (2010). Reliability and validity of the Turkish version of the shorter form of the gagging problem assessment questionnaire. Journal of Oral Rehabilitation, 37: 21–25.

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

American Psychiatric Association (2000). Diagnostic and statistical manual of mental disorders (4th ed). (DSM-IV-TR). Washington, DC.

Armfield, J.M., Stewart, J.F. & Spencer, A.J. (2007). The vicious cycle of dental fear: exploring the interplay between oral health, service utilization and dental fear. BMC Oral Health, 7: 1.

Armfield JM (2010). Towards a better understanding of dental anxiety and fear: cognitions vs. experiences. European Journal of Oral Sciences, 118: 259–264.

Arntz, A., de Groot, C. & Kindt, M. (2005). Emotional memory is perceptual. Journal of Behavior Therapy and Experimental Psychiatry, 36: 19–34.

Bassi, G.S., Humphris, G.M. & Longman, L.P. (2004). The etiology and management of gagging: a review of the literature. The Journal of Prosthetic Dentistry, 91: 459–467.

Boomsma, D.I., de Geus, E.J., Vink, J.M., et al. (2006). Netherlands twin register: from twins to twin families. Twin Research and Human Genetics, 9: 849–857.

Boomsma, D., Busjahn, A. & Peltonen, L. (2002). Classical twin studies and beyond. Nature Reviews. Genetics, 3: 872-82.

Cohen, S.M., Fiske, J. & Newton, J.T. (2000). The impact of dental anxiety on daily living. British Dental Journal, 189: 385-390.

Cuthbert, B. N., Lang, P. J., Strauss, C., Drobes, D., Patrick, C. J. & Bradley, M. M. (2003). The psychophysiology of anxiety disorder: Fear memory imagery. Psychophysiology, 40: 407–422.

De Jongh, A., Oosterink, F.M.D., Kieffer, J.M., Hoogstraten, J. & Aartman, I.H.A. (2011). The Structure of Common Fears: Comparing Three Different Models. The American Journal of Psychology, 124: 141-149.

De Jongh, A., Bongaarts, G., Vermeule, I., Visser, K., De Vos, P. & Makkes, P. (1998). Blood-injury-injection phobia and dental phobia. Behaviour Research and Therapy, 36: 971-82.

De Quervain, D. J., Aerni, A., Schelling, G. & Roozendaal, B. (2009). Glucocorticoids and the regulation of memory in health and disease. Frontiers in Neuroendocrinology, 30: 358–370.

De Quervain, D.J., Kolassa, I.T., Ertl, V., Onyut, P.L., Neuner, F., Elbert, T. & Papassotiropoulos, A. (2007). A deletion variant of the alpha2b-adrenoceptor is related to emotional memory in Europeans and Africans. Nature Neuroscience, 10: 1137-1139.

Elsesser, K., Heuschen, I., Pundt I & Sartory, G. (2006). Attentional bias and evoked heart-rate response in specific phobia. Cognition and Emotion, 20: 1092–1107.

Erten, H., Akarslan, Z.Z. & Bodrumlu, E. (2006). Dental fear and anxiety levels of patients attending a dental clinic. Quintessence International (Berlin, Germany: 1985), 37: 304-310.

Fredrikson M, Annas P, Fischer H, et al. (1996). Gender and age differences in the prevalence of specific fears and phobias. Behaviour Research and Therapy, 34: 33–39.

Hakeberg, M., Berggren, U. & Carlsson, S. G. (1992). Prevalence of dental anxiety in an adult population in a major urban area in Sweden. Community Dentistry and Oral Epidemiology, 20: 97–101.

Halonen H., Salo T., Hakko, H. & Räsänen P. (2014). The association between dental anxiety, general clinical anxiety and depression among Finnish university students. Oral Health and Dental Management, 13: 320-325.

Hettema, J. M., Neale, M. C. & Kendler, K. S. (2001). A review and meta-analysis of the genetic epidemiology of anxiety disorders. American Journal of Psychiatry,158: 1568–1578.

Hill, K.B., Chadwick, B., Freeman, R., O'Sullivan, I. & Murray, J.J. (2013). Adult Dental Health Survey 2009: relationships between dental attendance patterns, oral health behaviour and the current barriers to dental care. British Dental Journal. 214: 25-32.

Humphris, G. & King, K. (2011). The prevalence of dental anxiety across previous distressing experiences. Journal of Anxiety Disorders, 25: 232-236.

Kendler, K. S., Karkowski, L. M. & Prescott, C. A. (1999). Fears and phobias: reliability and heritability. Psychological Medicine, 29: 539–553.

Kindt M. & Soeter M. (2011). Reconsolidation in a human fear conditioning study: a test of extinction as updating mechanism. Biological Psychology, 92: 43-50.

Klingberg, G. & Broberg, A. G. (2007). Dental fear/anxiety and dental behaviour management problems in children and adolescents: a review of prevalence and concomitant psychological factors. International Journal of Pediatric Dentistry, 17: 391–406.

Leutgeb, V., Schafer, A. & Schienle, A. (2011). Late cortical positivity and cardiac responsitivity in female dental phobics when exposed to phobia-relevant pictures. International Journal of Psychophysiology. 79: 410–416.

Locker, D., Liddell, A., Dempster, L. & Shapiro D. (1999). Age of onset of dental anxiety. Journal of Dental research, 78: 790-796.

Locker, D. (2003). Psychosocial consequences of dental fear and anxiety. Community Dentistry and Oral Epidemiology, 31: 144–151.

McGaugh, J.L. (2004). The amygdala modulates the consolidation of memories of emotionally arousing experiences. Annual Review of Neuroscience, 27: 1-28.

McIntyre, C.K. & Roozendaal, B. (2007). Neural Plasticity and Memory: From Genes to Brain Imaging. Chapter 13: Adrenal Stress Hormones and Enhanced Memory for Emotionally Arousing Experiences. Bermúdez-Rattoni F., editor, Boca Raton (FL): CRC Press.

Mehrstedt, M., John, M.T., Tönnies, S. & Micheelis, W. (2007). Oral health-related quality of life in patients with dental anxiety. Community Dentistry and Oral Epidemiology, 35: 357-63.

Mineka, S. & Ohman, A. (2002). Born to fear: non-associative vs associative factors in the etiology of phobias. Behaviour Research and Therapy, 40: 173-184.

Moore, R., Brødsgaard, I. & Birn, H. (1991). Manifestations, acquisition and diagnostic categories of dental fear in a self-referred population. Behaviour Research and Therapy, 29: 51–60.

Nicolas, E., Collado, V., Faulks, D., Bullier, B. & Hennequin, M. (2007). A national cross-sectional survey of dental anxiety in the French adult population. BMC Oral Health, 7: 12.

Oosterink, F. M. D., De Jongh, A. & Hoogstraten, J. (2009). Prevalence of dental fear and phobia relative to other fear and phobia subtypes. European Journal of Oral Sciences, 117: 135–143.

Oosterink, F. M.D., De Jongh, A. & Aartman, I.H.A. (2008). What are people afraid of during dental treatment? Anxiety-provoking capacity of 67 stimuli characteristic of the dental setting. European Journal of Oral Sciences, 116: 44–51.

Öst, L. G. (1987). Age of onset in different phobias. Journal of Abnormal Psychology, 96: 223-229.

Öst, L.G., Sterner, U., Lindhahl, I.L. (1984). Psychological responses to blood phobics. Behaviour Research and Therapy, 22: 109–117

Packer, M.E., Joarder, C., Lall, B.A. (2005). The use of relative analgesia in the prosthetic treatment of the 'gagging' patient. Dental Update, 32: 544, 548-546, 550.

Page, A.C. (1994). Blood-injury phobia. Clinical Psycology Review, 14: 443–461.

Pratt, D., Cooper, M.J. & Hackmann, A. (2004). Imagery and its characteristics in people who are anxious about spiders. Behavioural and Cognitive Psychotherapy, 32: 165–176.

Poulton, R. & Menzies, R. G. (2002). Non-associative fear acquisition: a review of the evidence from retrospective and longitudinal research. Behaviour Research and Therapy, 40: 127–149.

Rachman, S. (1977). The conditioning theory of fear-acquisition: a critical examination. Behaviour Research and Therapy, 15: 375–387.

Sari, E. & Sari, T (2010). The role of acupuncture in the treatment of orthodontic patients with a gagging reflex: a pilot study. British Dental Journal, 208: E19.

Schuller, A.A., Willumsen, T. & Holst, D. (2003). Are there differences in oral health and oral health behavior between individuals with high and low dental fear? Community Dentistry and Oral Epidemiology, 31: 116-121.

Singer, R., Cardenas, G., Xavier, J., Jeanty, Y., Pereyra, M., Rodriguez, A. & Metsch, L.R. (2012). Dental anxiety and the use of oral health services among people attending two HIV primary care clinics in Miami. Public Health Reports;127 Suppl 2: 36-44.

Smith, T.A. & Heaton, L.J. (2003) Fear of dental care: are we making any progress? Journal of the American Dental Association (1939). 134: 1101-1108.

Stinson, F.S., Dawson, D.A., Patricia Chou, S., Smith, S., Goldstein, R.B., June Ruan & W., Grant, B.F. (2007). The epidemiology of DSM-IV specific phobia in the USA: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Psychological Medicine, 37: 1047-1059.

Stouthard, M. E. A. & Hoogstraten, J. (1990). Prevalence of dental anxiety in the Netherlands. Community Dentistry and Oral Epidemiology, 18: 139–142.

Uziel, N., Bronner, G., Elran, E. & Eli, I. (2012). Sexual correlates of gagging and dental anxiety. Community Dental Health, 29: 243–247.

Van den Heuvell, G. F. E. C. V. L., Ter Pelkwijk, B. J. & Stegenga, B. (2008). Development of the gagging problem assessment: A pilot study. Journal of Oral Rehabilitation, 35: 196-202.

Vassend, O., Røysamb, E. & Nielsen, C. S. (2011). Dental anxiety in relation to neuroticism and pain sensitivity. A twin study. Journal of Anxiety Disorders, 25: 302–308.

Vassend, O. (1993). Anxiety, pain and discomfort associated with dental treatment. Behaviour Research and Therapy, 31: 659-666.

Vermaire, J.H., Houtem, C.M.H.H. van, Ross, J,N., Schuller, A.A. (in press). The burden of disease of dental anxiety; generic and disease-specific quality of life in patients with and without extreme levels of dental anxiety. European Journal of Oral Sciences. DOI: 10.1111/eos.12290.

Vermaire, J.H., De Jongh, A. & Aartman I.H. (2008). Dental anxiety and quality of life: the effect of dental treatment. Community Dentistry and Oral Epidemiology, 36: 409-16.

Winocur, E., Uziel, N., Lisha, T., Goldsmith, C. & Eli, I. (2011). Self-reported Bruxism – associations with perceived stress, motivation for control, dental anxiety and gagging. Journal of Oral Rehabilitation, 38: 3–11.

Wong, H.M., Mak, C.M. & To,W.M. (2015). Development of a Dental Anxiety Provoking Scale: A pilot study in Hong Kong. Journal of Dental Sciences, 10: 240-247.

I have two brothers and three sisters. All of us but one are afraid of the dental treatment. Besides that, I am also afraid of closed spaces and bats. Is anxiety heritable?

CHAPTER 2

A review and meta-analysis of the heritability of specific phobia subtypes and corresponding fears

C.M.H.H. van Houtem, M.L. Laine, D.I. Boomsma,
L. Ligthart, A.J. van Wijk, A. de Jongh

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Introduction

It is estimated that more than 40% of the general population suffers from one or more fears of a specific object or situation at some times in their lives (Oosterink et al., 2009; Depla et al., 2008; Curtis et al., 1998). If a fear becomes excessive or unreasonable it is termed a phobia (American Psychiatric Association, 2000). Specific phobia is an anxiety disorder that is defined as an unreasonable or irrational fear which has a significant negative impact on daily living (APA, 2000). With life-time prevalence rates of over 10% (LeBeau et al., 2010; Kessler et al., 2005), specific phobias are the most prevalent group of mental disorders. A specific phobia is a common, long lasting, often chronic anxiety disorder (Depla et al., 2008; Goisman et al., 1998), associated with serious impairment (Oosterink et al., 2009; Alonso et al., 2004; Magee et al., 1996) that represents a serious public health problem with a substantial economic burden (Alonso et al., 2004; Greenberg et al., 1999; Robins et al., 1984).

The DSM-IV-TR (APA, 2000) distinguishes five main categories or subtypes of specific phobia: animal type, natural environment type, situational type, blood–injury–injection type, and "other" type. The subtypes of specific phobia differ in terms of prevalence, sex distribution and age of onset. Women appear to have higher prevalence rates of fears and specific phobias in general than men (Oosterink et al., 2009b; Lipsitz et al., 2001; Fredrikson et al., 1996; McNally, 1994). In the natural environment, animal, blood–injury subtype and other type (i.e., emetophobia ("vomiting phobia"); Czajkowski et al., 2011; Depla et al., 2008; Lipsitz et al., 2001) the age of onset varies between 8 and 13 years, while in the situational subtype this appears to be higher (14–15 years; Depla et al., 2008).

There is a common theory that the development of fears and specific phobias can best be understood by application of the behavioral paradigm or classical conditioning model; that is, the pairing of an indifferent stimulus, conditioned stimulus (CS) with an unconditioned stimulus (US) which automatically evokes a fear response (e.g., Davey, 1997). Conditioning theories state that objects and situations which are irrationally feared, resemble previous distressing experiences (e.g., pain). Yet, not all phobia subtypes develop according to the principle of classical conditioning alone. For example, animal phobias (e.g., spiders, mice, bats, etc.), and phobias of the natural environment type (e.g., water phobia), have not been found to be the result from experiences associated with pain or terror (Menzies & Clarke, 1993). An influential model concerning the development of fears and phobias states that specific phobias are not only acquired through traumatic conditioning experiences, but also through transmission of information and observational learning (Rachman, 1977). For some fear and specific phobia subtypes, the contribution of these pathways does not appear to be substantial or is even lacking (e.g., King et al., 1998). A study that aimed to maximize the prediction of a current specific phobia diagnosis by using combinations of distressing experiences, including those based on modeling and negative information, show that these

accounted for less than 50% of the variance (Oosterink et al., 2009). Such findings cast doubt on the validity of conditioning, modeling, and information pathways as the sole explanation of how specific phobias develop, and have inspired others to develop a so-called non-associative account of phobic etiology (Poulton & Menzies, 2002). This theory assumes that a number of fears have an evolutionary background and pertain to stimuli that once posed a challenge to the survival of mankind.

The observation that conditioning processes are not always necessary for the acquisition of a fear and thus for a number of specific phobias implies that other innate factors, including genetic susceptibility, may play a role in the development of specific phobias (Hettema, Neale & Kendler, 2001). The model that describes this combination of genetic and environmental influences is the diathesis-stress model of illness (Monroe & Simons, 1991). This model attempts to explain behaviors or psychological disorders as a result of the interaction of genetic vulnerability or predisposition (diathesis) with the environment and life events (stressors). According to this classical model, there is an inverse relationship between the level of genetic liability and the level of onset-related environmental stressors (Jang, 2005).

To determine whether there is a familial component to fears and phobias, studies have been conducted that showed aggregation within families (Depla et al., 2008; Hettema et al., 2001; Fyer et al., 1995). Once familial aggregation is observed, twin or adoption studies test to what extent familiarity is explained by shared genetic factors or shared family environment. In twin studies the resemblance of monozygotic (MZ) and dizygotic (DZ) twin pairs is compared. Identical or monozygotic (MZ) twins, being male–male (MM) or female–female (FF) pairs, share (nearly) 100% of their genes, while non-identical or dizygotic (DZ) twins, which can be MM, FF or MF (male–female or opposite sex, OS) share on average 50% of their segregating genes. The variation in liability to a disorder or trait can be described to four potential sets of effects: additive genetic effects (A), non-additive or dominant genetic effects (D), family or common environmental effects (C; e.g., events, conditions or experiences that are common to all members of a household) and individual specific or unique environmental effects (E; e.g., individual events). A, D and C all contribute to resemblance of MZ and DZ twins, whereas E does not. Since MZ twins are (nearly) genetically identical, any differences between them will be the result of non-shared environmental factors. If the correlation in MZ twins exceeds the correlation in DZ twins this indicates additive genetic effects on this trait or disorder, and if the correlation in MZ twins is more than twice the correlation in DZ twins there is also evidence for non-additive genetic influences (D). Shared environmental factors, on the other hand, will cause the same degree of resemblance in MZ and DZ twins, because both types of twins share these environmental factors to the same extent. Based on these principles, it is possible to disentangle the effects of non-shared environmental, shared environmental and genetic factors on a trait.

A meta-analysis, conducted more than 10 years ago, suggested that phobias are moderately heritable with an estimated heritability ranging from 20% to 40% (Hettema et al., 2001). However, in this study within each of the individual categories, specific phobias were grouped together with the other main categories of phobias (i.e., social phobia, generalized social phobia, and agoraphobia), making it difficult to estimate the variance explained by genetic factors for specific phobia per se (Hettema et al., 2001). To provide an overview and update of the current knowledge regarding the heritability of specific phobias and their corresponding fears, the aims of this study are (1) to review the current literature of twin studies regarding the genetic basis of specific phobias and their corresponding fears and (2) to conduct a meta-analysis of published twin studies in order to provide an estimate of the genetic and environmental influences of the different subtypes of specific phobias and fears.

Methods

A systematic search of the published literature (MEDLINE-PubMed) was conducted for all studies published between 1967 and April 2012 to select relevant twin studies describing the heritability of specific phobias and their corresponding fears. Combinations of the following search themes were used: “fear, genetic(s)”; “phobia, genetic(s)”; “fear, heritability” and “phobia, heritability”. Abstracts of these search results were examined and relevant full text articles were retrieved for review. The reference lists and citations were examined to identify any eligible report not previously located through the database search.

Criteria for inclusion and exclusion of relevant articles were determined a priori and assessed. Articles were included when they described a twin study in an adult population and contained information on estimated heritability of any fear or specific phobia subtype. Studies reporting on other anxiety disorders (e.g., panic disorder with/without agoraphobia) were included only when a fear or specific phobia was reported as a comorbid anxiety disorder and when data on estimated heritability were available for inclusion. Articles that aimed to describe specific phobias, but which used a fear measure, such as the Fear Questionnaire (Fredrikson et al., 1996) rather than a psychological assessment procedure, like the Structured Clinical Interview for DSM Disorders (SCID; First et al., 2002) or Composite International Diagnostic Interview (CIDI; Robins et al., 1988), are described separately. We excluded studies that depended on electrodermal skin conductance (i.e., Hettema et al., 2003) or other non-specific diagnostic tools without additional psychological assessment. Literature reviews were excluded. Studies including only social phobia or agoraphobia without co-morbid specific phobias were excluded as these phobias do not belong to the category of specific phobias according to DSM-IV-TR (APA, 2000). Furthermore, studies measuring the stable component of heritability across assessment times (Kendler et al., 1999)

were excluded since these stand apart from the single assessment studies, and already represents a type of 'meta-analysis' obtained by structural equation analysis as applied to a measurement model. Studies using a rater-bias model (Kendler et al., 2008) were also excluded since the heritability obtained thereby is not comparable to those obtained from standard twin studies. Candidate gene studies and genetic association studies (regarding the effects of specific genes on a trait, rather than estimates of heritability) were beyond the scope of this review and were therefore excluded.

From each included study, whenever possible, the lead author, year of publication, demographics, sample size, fear or specific phobia subtype, assessment instrument, correlation in MZ and DZ twins, heritability estimates and best fit model were extracted. A meta-analysis was conducted for different fears and specific phobia subtypes (i.e., animal, situational, blood–injury–injection and miscellaneous) by averaging the estimates of the additive genetic (A), dominant genetic (D), common environmental (C), and unique environmental (E) variance components estimates weighted by the sample size according to Sutton (Sutton et al., 2000; see also Verweij et al., 2010; Li et al., 2003) in order to give more powerful studies greater influence. Calculations were conducted in Microsoft Office Excel2007. Estimates were made separately for each phenotype (fear or specific phobia subtype) when at least two independent studies estimated a variance component for that phenotype. Forest plots could not be created since only a limited number of studies (i.e., for fear Vassend et al., 2011; i.e., for specific phobia subtypes Kendler et al., 2002; Kendler et al., 2001) reported the necessary information. If studies were based on the same cohort and also reported heritability estimates of the same specific phobia subtype (i.e., Hettema et al., 2006; Hettema et al., 2005; Kendler et al., 2003), the study with a focus being most in line with the scope of our review was selected and included in the meta-analysis (i.e., Hettema et al., 2005). Reported estimated heritabilities of the non-specified "any phobia" category were excluded. One study was excluded, because the phobia subtypes investigated did not relate to any official specific phobia subtype (i.e., blood–needle–hospital and blood–needle–hospital–illness; Neale et al., 1994). Due to the scarcity of studies on fear and phobia subtypes for which the male–female ratio was reported, it was not possible to conduct separate meta-analyses for the heritability in both sexes.

Results

General

The search themes "fear, genetic" identified a total of 1356 manuscripts, "fear, genetics" identified 2255 hits, "phobia, genetic" identified a total of 308 hits, and "phobia, genetics" identified 424 hits. "Fear, heritability" produced 29 hits and "phobia, heritability" 31 hits.

The search strategy resulted in 4403 titles. After screening 15 articles were included. Ten of them were included in the meta-analysis. The study selection process is detailed in Fig. 1. Five articles met our inclusion criteria for a fear study. Table 1 summarizes the characteristics of the eligible studies on fears. Ten articles fulfilled the criteria for a specific phobia study. In Table 2 the characteristics of the eligible studies on specific phobias are characterized. No adoption studies on fears and phobias were found. No additional articles were found by consulting publications cited by other articles and reference lists of other articles.

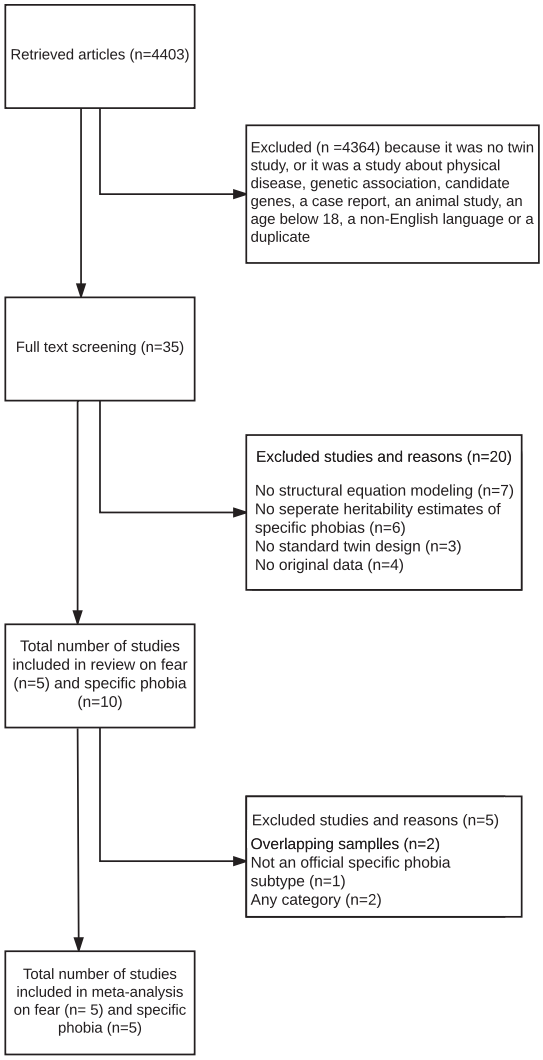

Fig. 1. Flowchart of studies included in review and meta-analysis

Twin studies of fears

Table 1 summarizes results from the five twin studies on fears. All of the studies included both genders. Two studies tested for qualitative sex effects (i.e., genetic factors that influence a trait are at least partially distinct in males and females), and quantitative sex effects (i.e., the same genetic factors impact to different degrees in males and females) (Distel et al., 2008; Kendler et al., 2008). A total of four studies used a population-based sample; one study was based on a clinical sample (Skre et al., 2000).

Page and Martin (1998) investigated the relative genetic and environmental contributions of three sets of variables to blood–injury–injection fears. Univariate analyses showed that with respect to blood fears nearly one third (29%) of the variance could be explained by unique environmental factors, and that the remaining part was associated with factors shared by family members.

In 2000, Skre et al. published a study using a relatively small clinical sample to examine the genetic and environmental contribution to common fears. For all the fear subtypes, except the combination of natural environment and situational fears, the correlations in MZ twins exceeded the correlations in DZ twins, suggesting the influence of genetic factors. It is difficult to evaluate the significance of these findings due to the low number of twin pairs and the absence of a comparison group from the general population.

Using a longitudinal study, Kendler et al. (2008) assessed the development of fears from adolescence to adulthood. Genetic and environmental risk factors for individual fears were found to be partly mediated through a common fear factor. With increasing age, total heritability for all four specific fears declined, but genetic influences on fears tended to be more specific in their effect. The best fit models had no quantitative or qualitative sex effects.

In a study of the Netherlands Twin Registry, Distel et al. (2008) examined the genetic and environmental influences in a large sample of Dutch twins on blood–injury, social and agoraphobic fears and assessed their interaction with gender and age. No sex differences were found in the influence of genetic effects. Genetic effects contributed to individual differences in blood–injury fears, with a broad-sense heritability estimate (i.e., additive plus non-additive genetic factors) of 36%. For all fears, there was support for a contribution of non-additive genetic influences. There was no evidence for genotype x sex interactions.

Vassend et al. (2011) examined dental anxiety in relation to neuroticism and pain sensitivity in a relatively small sample. Dental anxiety proved moderately heritable. A considerable overlap between the factors that influence individual variation in neuroticism, and those that affect liability to dental anxiety was found. Because of the low statistical power it is difficult to evaluate the significance of these findings.

Table 1. Twin studies on fears

Study	Population & sample	Mean age (years ± SD)	Gender	Number of twins (cases and controls)	Subtype fear	Assessment instrument	*R*mz	*R*dz	A	D	C	E	Genetic Model
Page & Martin (1998)	Australian Population based	45.2 (±11.2)	M, F	659 twin pairs	Blood	Three questions about blood-injections injury fears	-	-	.71	-	-	.29	AE
Skre et al. (2000)	Norwegian Clinical based	41 (±9)	M, F	61 twin pairs (cases)	Any	Fear questionnaire[a]	.46	.25	.16	-	-	0.84	AE
					Animal		.55	.14	.47	-	-	0.53	AE
					Natural environment/ situational		.37	.56	-	-	.21	0.79	CE
					Blood-injection-injury		.19	-.08	.02	-	.00	0.98	ACE[f]
Kendler et al. (2008b)	Swedish Population based	19-20	M, F	1705	Animal	Fear questionnaire[b]	.55 M .52 F	.39 M .30 F .09 OS	.45	-	-	0.55	AE
					Blood-injury	Fear questionnaire[b]	.36 M .36F	.16 M .12 F .23 OS	.39	-	-	0.61	AE
					Situational	Fear questionnaire[b]	.50 M .36 F	.40 M .13 F .16 OS	.41	-	-	0.59	AE
Distel et al. (2008)	Dutch Population based	14-65 26-65	M, F	7089 2814	Blood-injury	Dutch version FQ[c]	Age 14-25 .33 Age 26-65 .39	Age 14-25 .13 Age 26-65 .09	.099	0.26	-	0.64	ADE
Vassend et al. (2011)	Norwegian Population based	23-35	M, F	188	Dental	NEO-PI-R[d] DAS[e]	.47	.23	.41	-	-	0.59	AE

Notes: *r*mz: MZ twin correlation; *r*dz: DZ twin correlation; A: additive genetic effects; C: common environmental effects; D: non-additive genetic effects; E: unique environmental effects; MM: male-male; FF: female-female; MF: male-female; OS, opposite-sex ;[a]Fear questionnaire (Torgersen, 1979); [b]Fear questionnaire developed by Fredrikson (Fredrikson et al., 1996); [c]FQ, Fear Questionnaire (Marks and Matthews, 1979); [d]NEO Personality Inventory Revised (Costa & McCrae, 1992); [e]Corah's Dental Anxiety Scale (Corah, 1969); [f]Violation of the assumption of equal variances in MZ and DZ twins.

Twin studies of specific phobias

Table 2 summarizes the results from ten twin studies on specific phobias that met the inclusion criteria. Of these studies, five included only women in their sample; one included only men and four were based on data from both males and females. All of the studies were population-based. The studies of Kendler et al. (1992), Kendler et al. (1993b), Neale et al. (1994) and Kendler et al. (1995) were based on the same sample of female twin pairs from the Virginia Twin Registry. The studies of Kendler et al. (2003), Hettema et al. (2005) and Hettema et al. (2006) reported on the same sample of male and female twins from the Virginia Twin Registry. Note that, while these studies report heritability estimates for partly the same traits based on the same or overlapping samples, the estimates differ slightly between studies because of differences in the models from which these were derived.

A large study examined the genetic epidemiology of phobias in female twins (Kendler et al., 1992). The results of the multivariate genetic analyses showed strong evidence supporting the presence of genetic and environmental risk factors unique to each phobia subtype, but also of genetic and environmental risk factors that would influence all phobia subtypes.

Kendler et al. (1993b) published another study based on the same sample with a similar design as in the study described above (Kendler et al., 1992). Their purpose was to test the equal environment assumption (i.e., the assumption that MZ and DZ twins are equally correlated for their exposure to environmental influences that are of etiologic relevance of a certain trait) in five common psychiatric disorders. The results in this study supported the equal environment assumption in these conditions.

Using a telephone interview, Neale and his colleagues (1994) investigated a condition termed “blood, needles, hospitals and illness (BNHI) phobia”. Unfortunately, it was not possible to choose a best fitting model, due to small differences in fit. The only model that was rejected was that of only unique environmental factors.

Kendler et al. (1995) examined the interrelationship between genetic and environmental risk factors for six psychiatric disorders (for study design, see Kendler et al., 1992). For specific phobia, the role of familial environment appeared to be of little importance.

Another population based study examined the sources of individual differences in risk of developing phobia subtypes in male twins (Kendler et al., 2001). Multivariate analyses suggested the presence of genetic and individual-specific environmental etiologic factors common to all phobia subtypes. Additionally, for each phobia subtype evidence was found for the presence of genetic and unique environmental factors specific to that phobia.

A similar study from the same research group examined sex differences in fears and phobias (Kendler et al., 2002). The low DZ-OS correlations (Table 2) suggested sex differences in these specific phobia subtypes. Although no support was found for the presence of quantitative and qualitative sex effects for animal phobia, the authors suggested for situational and blood/injury phobia the presence of qualitative sex effects.

Table 2. Twin studies on specific phobias

Study	Population & sample	Mean age (years± SD)	Gender	Number of twins (cases and controls)	Subtype phobia	Assessment instrument	*r*mz	*R*dz	A	D	C	E	Genetic Model
Kendler et al. (1992)	American Population based	30.1 (± 7.1)	F	2163	Any	Phobic disorders section DIS-III-A[a]	.32	.15	.32	-	-	.68	AE
					Animal	Phobic disorders section DIS-III-A[a]	.38	.04	.32	-	-	.68	AE
					Situational	Phobic disorders section DIS-III-A[a]	.27	.27	-	-	.27	.73	CE
Kendler et al. (1993b)	American Population based	30.1 (± 7.1)	F	2163	Any	Phobic disorders section DIS-III-A[a]	-	-	.28	-	-	.72	AE
Neale et al. (1994)	American Population based	30.1 (± 7.1) years + 17.8 (±3.8) months	F	1858	Blood Needle Hospital Illness	Phobic disorders section DIS-III-A[a]	.33	.33	.057	-	.28	.66	ACE[d]
					Blood Needle Hospital	Phobic disorders section DIS-III-A[a]	.30	.29	.049	-	.26	.69	ACE[d]
Kendler et al. (1995)	American Population based	30.1 (± 7.1)	F	2163	Any	Phobic disorders section DIS-III-A[a]	-	-	.35	-	.02	.63	ACE
Kendler et al. (2001)	American Population based	36.8 (±9.1) (age range 20-58)	M	1198 twin pairs and 544 individual twins	Animal	Phobic disorders section DIS-III-A[a]	-	-	.35	-	-	.65	AE
					Situational	Phobic disorders section DIS-III-A[a]	-	-	.25	-	-	.75	AE
					Blood-injury	Phobic disorders section DIS-III-A[a]	-	-	.28	-	-	.72	AE
					Any	Phobic disorders section DIS-III-A[a]	-	-	.22	-	-	.78	AE

Table 2. Twin studies on specific phobias (*continued*)

Study	Population & sample	Mean age (years± SD)	Gender	Number of twins (cases and controls)	Subtype phobia	Assessment instrument	*r*mz	*R*dz	A	D	C	E	Genetic Model
Kendler et al. (2002)	American Population based	36.3(±8.2) (FF) 37.0(±9.1) (MF/MM)	M, F	7569	Animal	Phobic disorders section DIS-III-A[a]	.40 M .37 F	.0.03 M .12 F .14 OS	.35	-	-	.65	AE
					Situational	Phobic disorders section DIS-III-A[a]	.35 M .38 F	.06 M .14 F .07 OS	.33	-	-	.67	AE AE
					Blood-injury	Phobic disorders section DIS-III-A[a]	.31 M .33 F	.13 M .05 F .05 OS	.30	-	-	.70	AE AE
Kendler et al. (2003)	American Population based	36.6(±8.1) (FF) 36.8(±9.1) (MM/MF)	M, F	>5600	Phobia	Phobic disorders section DIS-III-A[a]	-	-	.16	-	.11	.73	ACE
					Situational	Phobic disorders section DIS-III-A[a]	-	-	.33	-	.01	.66	ACE
					Animal	Phobic disorders section DIS-III-A[a]	-	-	.22	-	.06	.71	ACE
Hettema et al. (2005)	American Population based	36.6(±8.1) (FF) 36.8(±9.1) (MM/MF)	M, F	>5000	Animal	DSM-III[b]	-	-	.24	-	.07	.69	ACE
					Situational	DSM-III [b]	-	-	.24	-	.02	.74	ACE
Hettema et al. (2006)	American Population based	36.6(±8.1) (FF) 36.8(±9.1) (MM/MF)	M, F	9270	Animal	DSM-III [b]	-	-	.20	-	0.09	.71	ACE
					Situational	DSM-III [b]	-	-	.16	-	.10	.73	ACE

Table 2. Twin studies on specific phobias (*continued*)

Study	Population & sample	Mean age (years± SD)	Gender	Number of twins (cases and controls)	Subtype phobia	Assessment instrument	*r*mz	*R*dz	A	D	C	E	Genetic Model
Czajkowski et al. (2011)	Norwegian Population based	28.1	F	1430	Any	CIDI[c]	-	-	-	-	-	-	-
					Animal		-	-	.44	-	-	.56	AE
					Natural environment/ situational				.43	-	-	.57	AE
					Blood-injection				.63	-	-	.37	AE

Notes: *r*mz: MZ twin correlation; *r*dz: DZ twin correlation; A: additive genetic effects; C: common environmental effects; E: unique environmental effects; MM: male-male; FF: female-female; MF: male-female; OS, opposite-sex; [a]modified. See for modifications (Kendler et al., 1992); [b]adaptation of the DSM-III criteria; [c]CIDI (Haro et al., 2006); [d]small difference in fit between models, not possible to choose between the different models.

Another study of Kendler et al. (2003) investigated lifetime diagnosis for 10 psychiatric syndromes in more than 5600 MZ and DZ male and female twins. No sex differences were found in the underlying structure of genetic and environmental risk factors.

Hettema et al. (2005) studied the liability of two subcategories of specific phobias: animal and situational. The pattern of genetic and environmental risk factors did not appear to differ significantly between both sexes.

In another study by Hettema and his colleagues the relationship between neuroticism and internalizing was examined (Hettema et al., 2006). The results of the multivariate analyses showed that in specific phobia condition-specific genetic and condition-specific unique environmental factors were substantial. The genetic correlation between neuroticism and animal phobia and situational phobia was 0.58 and 0.74, respectively. Effects were roughly the same in men and women.

Czajkowski et al. (2011) published a population-based study about the structure of genetic and environmental risk factors for phobias in women. Co-occurrence between phobia subtypes could be explained by two common liability factors. Genetic risk factors for complex phobias and animal phobias were largely distinct.

Meta-analyses of twin studies

Table 3 shows the results of the meta-analyses. Results for fears in the meta-analyses of parameters of h^2 (heritability), c^2 (common environment) and e^2 (unique environment) were derived from five independent studies (Vassend et al., 2011; Distel et al., 2008; Kendler et al., 2008; Skre et al., 2000; Page & Martin, 1998). For specific phobias results were included from five independent studies (Czajkowski et al., 2011; Hettema et al., 2005; Kendler et al., 2002, 2001, 1992). For fears estimated heritabilities were calculated for the animal, blood–injury–injection and miscellaneous categories. For specific phobias estimated heritabilities were determined for the animal, situational and blood–injury–injection subtypes. As none of the studies contained data about the natural-environment and the 'other' specific phobia subtypes, these categories are absent in Table 3. The highest mean heritability (±SEM) for fear subtypes was found for animal fear (45% ± 0.004), and the highest mean heritability for the specific phobia subtypes that was identified was for the blood–injury–injection subtype (33% ± 0.06).

Discussion

The present study sought to go beyond the limitations of a prior review and meta-analysis that did not distinguish specific phobias from other types of phobias (Hettema et al., 2001), and attempted to derive a current estimate of the heritability of fears and specific phobia

Table 3. Summary of findings included in the meta-analysis

Phenotype	Fear studies included in analyses	Phobia studies included in analyses	Range heritability fear	Range heritability specific phobia	Mean heritability fear % (±SEM)	Mean heritability specific phobia % (±SEM)	Genetic model
Animal	Skre et al. (2000) Kendler et al.(2008b)	Kendler et al. (1992) Kendler et al. (2001) Kendler et al. (2002) Hettema et al. (2005) Czajkowski et al. (2011)	45-47	22-44	45 (0.004)	32 (0.03)	AE/ACE
Situational	-	Kendler et al. (1992) Kendler et al. (2001) Kendler et al. (2002) Hettema et al. (2005)	-	0-33	-	25 (0.05)	AE/ACE/CE
Blood-injury injection	Page & Martin (1998) Skre et al. (2000) Kendler et al.(2008b) Distel et al. (2008)	Kendler et al. (2001) Kendler et al. (2002) Czajkowski et al. (2011)	2-71	28-63	41 (0.06)	33 (0.06)	AE/ACE/ADE
Miscellaneous*	Skre et al. (2000) Vassend et al. (2011)	-	0-41	-	25 (0.14)	-	AE/CE

Notes: A: additive genetic effects; C: common environmental effects; D: non-additive genetic effects; E: unique environmental effects; SEM: standard error of mean; * other fears (i.e., dental and a combination of natural environment/situational)

subtypes. Since the study of Hettema et al. (2001) only five publications reporting heritability estimates on specific phobias, and three reporting heritability estimates on fears were published. As far as we know, no review pertained to heritability estimates of fears alone.

The results of our study suggest that specific phobias and their corresponding fears are moderately heritable with rates that vary across subtypes. The estimated heritability of fears and specific phobias falls within the range of 0–71% with the lowest estimate for the miscellaneous fear subtype (0%), and the highest estimates for the category of blood–injury–injection fears (71%) and phobias (63%; Table 3). The data converge on the conclusion that there is familial vulnerability to the phenotypic expression of particular types of fears and specific phobias. Other than additive genetic effects, unique environmental effects appear to explain most of the variance, whereas the influence of common environmental effects seems to be relatively modest. In this respect it is important to note that the data on estimated heritability of fears are not to be much different from those on phobias. This is on par with findings of research aimed at delineating the multidimensional structure of fears suggesting that the structure of subclinical fears can be inferred from the DSM classification of phobia subtypes and that fears and phobias are two observable manifestations of a fear response along a single continuum (De Jongh et al., 2011).

Findings of this meta-analysis are largely in line with those derived by Hettema et al. (2001), albeit they found somewhat more variation with regard to the influence of additive genetic effects compared to the present study. One possible explanation for the differences between the heritability estimates of both meta-analyses relates to sample characteristics of the studies being reviewed. For example, the present review included “pure” samples of individuals who met DSM criteria for specific phobias, in contrast to samples of specific phobia that were grouped together with social phobia and/or agoraphobia (e.g., Tambs et al., 2009). A second explanation for the differences with the previous review relates to the fact that many studies used diagnostic instruments that are incapable of assessing the diagnostic features of specific phobia. For this reason, relatively stringent criteria for distinguishing between fears and specific phobias were applied in the present study.

The results of the present study suggest that unique environments, such as conditioning events, personal life events and other personal psychosocial stress factors, can have robust influences on the development of phobias. This mirrors earlier findings (Gregory et al., 2008; Hettema et al., 2001), and investigations on the concept of neuroticism (Eysenck & Eysenck, 1975), and the presence of a human fear conditioning trait (Hettema et al., 2003). These views predict that there are individual differences in the tendency to respond to exposure to a certain event (Andrews et al., 1994; Carey, 1990). According to this line of reasoning, the underlying genetics of specific phobias would explain why one individual reacts with more worry and catastrophic expectations and associated arousal during a conditioning experience than another, and how this makes some individuals more vulnerable to acquire a fear

or specific phobia than others. Thus, genetic factors may moderate the effect of individuals' confrontations with a phobic stimulus by influencing the extent to which fear associations are acquired, a process that may depend on the type of fear or specific phobia involved. This view is supported by the results of a study among 173 same sex twin pairs (90 MZ and 83 DZ) using a fear conditioning paradigm during which pictures of spiders and snakes as well as of triangles and circles were paired with mild electric shocks (Hettema et al., 2003). The fear conditioning process was found to be moderately heritable, accounting for 35–45% of the variability in electrodermal skin conduction. Further, the authors found some support for the notion that the heritability of the fear response to evolutionary fear-relevant stimuli spiders and snakes is higher than to geometric shapes. This would be in line with evolutionary theories predicting that people are primed to automatically and selectively attend to specific stimuli that are important to survival, thereby making these fears easily conditioned and relatively difficult to extinguish (LoBue et al., 2010; Menzies et al., 1998; Menzies & Clarke, 1995). According to Menzies and Clarke's non-associative model of fear acquisition, fears of long-standing natural dangers to the species (e.g., height phobia) can be acquired without any direct conditioning, whereas direct conditioning would play a prominent role in fears of relatively recent stimuli, such as motor cars (in the case of driving phobia), dental drills (in the case of dental phobia), airplanes (in the case of flight phobia) and hypodermic needles (in case of injection phobia), for which evolution has not yet have directly protected the species. According to this model, the latter stimuli should have the highest conditioning rates according to this model (Menzies & Clarke, 1995). Unfortunately, the present data are insufficiently detailed and too scarce to provide support for this hypothesis.

In general, women report higher prevalence rates of fears and specific phobias than men (Oosterink et al., 2009; Oosterink et al., 2009; Lipsitz et al., 2001; McNally, 1994). However, no support was found for the presence of sex differences in genetic contribution to fears and specific phobias. The failure to detect sex differences for anxiety disorders maybe due to limited statistical power of the studies (Kendler et al., 2002), but may also be considered as evidence for the contention that the same genes affect fear in men and women (Distel et al., 2008).

Several potential limitations of this study should be noted. First, the lack of power in some studies threatened their internal and external validity. For instance, in the study of Neale et al. (1994) only 124 subjects suffered from a specific phobia and only 11 of them reported an 'illness phobia'. Second, the DSM category of specific phobias is a diagnostically heterogeneous class of conditions, even within the subtypes. This is particularly relevant when one considers how fears have been grouped in previous genetic studies (e.g., Kendler et al., 1999). For example, when evolutionarily-relevant (e.g., blood–injury) and evolutionarily neutral (e.g., dental) fears are collapsed, it becomes potentially difficult to assess heritability differences among these fears in case these would exist. Even more obscuring is

the fact that some fears are in themselves a repository of fears that each may differ in terms of genetic and environmental variability. An example of such heterogeneity within the fears domain is the wide array of fears that pertain to the dental treatment setting, such as fear of pain experience, gagging or suffocating, drilling in or extractions of teeth, receiving a dental injection, having a root canal treatment, and 60 other potential fear-evoking objects and situations (see Oosterink et al., 2008, for an overview). Thus, like many other fears, fear of dental treatment might actually be the expression of a series of other underlying fears which possess features that distinguish them from each other. Third, the heritable part of specific phobia should be considered polygenetic (see also Stewart & Pauls, 2010; Broekman et al., 2007, for similar arguments in relation to other types of anxiety disorders). Related to this is the fact that specific phobia subtypes are highly comorbid with other anxiety disorders (Trumpf et al., 2010; Tambs et al., 2009; Depla et al., 2008; Kessler et al., 2005; Curtis et al., 1998; Magee et al., 1996; Kendler et al., 1993a), suggesting a shared genetic vulnerability (Middeldorp et al., 2005).

Conclusions

The present paper provides a state-of-the-art overview of the available evidence on the heritability of specific phobias and fears. It is a dissatisfying observation to find that data on the genetic contribution to fears and specific phobias are still scarce. Since many of the studies appear to represent data from the same subject populations, the meta-analysis represents results of only few studies. In addition, only five twin studies pertained to specific phobia, whereas the other five studies focused on the heritability of specific phobia as a comorbid anxiety disorder. Because of these limitations it is difficult to draw definitive conclusions on the basis of this meta-analysis. Therefore, perhaps the most notable conclusion of the present review is the need for additional research, examining a wider array of fear and phobia subtypes, using proper diagnostic assessment instruments, a clear sex distribution and large sample sizes.

References

Alonso, J., Angermeyer, M. C., Bernert, S., Bruffaerts, R., Brugha, T. S., Bryson, H., et al.(2004). Use of mental health services in Europe: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. Acta Psychiatrica Scandinavica, 109: 47–54.

Andrews, G., Crino, R., Hunt, C., Lampe, L. & Page, A. (1994). The treatment of anxiety disorders: clinician's guide and patient manuals. New York: Cambridge.

American Psychiatric Association. (2000). Diagnostic and statistical manual of mental disorders. 4th ed. (DSM-IV-TR). Washington, DC.

Broekman, B. F., Olff, M. & Boer, F. (2007). The genetic background to PTSD. Neuro-science and Biobehavioral Review, 31: 348–362.

Carey, G. (1990). Genes, fears, phobias, and phobic disorders. Journal of Counseling and Development,68: 628–632.

Corah, N. L. (1969). Development of a dental anxiety scale. Journal of Dental Research, 48: 596.

Costa, P. T. & McCrae, R. R. (1992). NEO PI-R professional manual. Odessa, FL: Psychological Assessment Resources.

Curtis, C. G., Magee, W. J., Eaton, W. W., Wittchen, H. U. & Kessler, R. C. (1998).Specific fears and phobias. Epidemiology and classification. British Journal of Psychiatry, 173: 212–217.

Czajkowski, N., Kendler, K. S., Tambs, K., Røysamb, E. & Reichborn-Kjennerud, T.(2011). The structure of genetic and environmental risk factors for phobias in women. Psychological Medicine, 41: 1987–1995.

Davey, G. C. L. (1997). A conditioning model of phobias. In: G. C. L. Davey (Ed.),Phobias, a handbook of theory, research and treatment (pp. 301–322). Chichester,UK: Wiley.

De Jongh, A., Oosterink-Wubbe, F., Hoogstraten, J., Kieffer, J. M. & Aartman, I. H.A. (2011). The structure of common fears: comparing three different models. American Journal of Psychology, 124: 141–149.

Depla, M. F. I. A., ten Have, ten, M. L., van Balkom, A. J. L. M. & de Graaf, R. (2008). Specific fears and phobias in the general population: results from the Netherlands Mental Health Survey and Incidence Study (NEMESIS). Social Psychiatry and Psychiatric Epidemiology, 43: 200–208.

Distel, M. A., Vink, J. M., Willemsen, G., Middeldorp, C. M., Merckelbach, H. L. G.J. & Boomsma, D. I. (2008). Heritability of self-reported Phobic Fear. Behavior Genetics, 38: 24–33.

Eysenck, H. J. & Eysenck, S. B. G. (1975). Manual of the Eysenck personality questionnaire. London: Hodder & Stoughton.

First, M. B., Spitzer, R. L., Gibbon, M. & Williams, J. B. W. (2002 November). Structured clinical interview for DSM-IV-TR Axis I Disorders, research version, patient edition.(SCID-I/P). New York: Biometrics Research, New York State Psychiatric Institute.

Fredrikson, M., Annas, P., Fischer, H. & Wik, G. (1996). Gender and age differences in the prevalence of specific fears and phobias. Behaviour Research and Therapy, 34: 33–39.

Fyer, A. J., Manuzza, S., Chapman, T. F., Martin, L. Y. & Klein, D. F. (1995). Specificity in familial aggregation of phobic disorders. Archives of General Psychiatry, 52: 564–573.

Goisman, R. M., Allsworth, J., Rogers, M. P., Warshaw, M. G., Goldenberg, I., Vasile, R.G., et al. (1998). Simple phobia as a comorbid anxiety disorder. Depression and Anxiety, 7: 105–112.

Greenberg, P. E., Sisitsky, T., Kessler, R. C., Finkelstein, S. N., Berndt, E. R., Davidson, J.R., et al. (1999). The economic burden of anxiety disorders in the 1990. Journal of Clinical Psychiatry, 60: 427–435.

Gregory, A. M., Lau, J. Y. F. & Eley, T. C. (2008). Finding gene–environment interactions for phobias. European Archives of Psychiatry and Clinical Neuroscience, 258: 76–81.

Haro, J. M., Arbabzadeh-Bouchez, S. & Brugha, T. S. (2006). Concordance of the Composite International Diagnostic Interview Version 3.0 (CIDI 3.0) with standardized clinical assessments in the WHO World Mental Surveys. International Journal of Methods in Psychiatric Research, 15: 167–180.

Hettema, J. M., Neale, M. C. & Kendler, K. S. (2001). A review and meta-analysis of the genetic epidemiology of anxiety disorders. American Journal of Psychiatry,158: 1568–1578.

Hettema, J. M., Annas, P., Neale, M. C., Kendler, K. S. & Fredrikson, M. (2003). A twin study of the genetics of fear conditioning. Archives of General Psychiatry, 60: 702–708.

Hettema, J. M., Prescott, C. A., Myers, J. M., Neale, M. C. & Kendler, K. S. (2005). The structure of genetic and environmental risk factors for anxiety disorders in men and women. Archives of General Psychiatry, 62: 182–189.

Hettema, J. M., Neale, M. C., Meyers, J. M., Prescott, C. A. & Kendler, K. S. (2006).A population-based twin study of the relationship between neuroticism and internalizing disorders. American Journal of Psychiatry, 163: 857–864.

Jang, K. L. (2005). The behavioral genetics of psychopathology: a clinical guide. Mahwah,NJ: Erlbaum Associates.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R. & Walters, E. E.(2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Archives of General Psychiatry, 62: 593–602.

Kessler, R. C., Chiu, W. T., Demler, O., Merikangas, K. R. & Walters, E. E. (2005).Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. Archives of General Psychiatry, 62: 617–627.

Kendler, K. S., Neale, M. C., Kessler, R. C., Heath, A. C. & Eaves, L. J. (1992). The genetic epidemiology of Phobias in Women. The Interrelationship of Agoraphobia, Social Phobia, Situational Phobia, and Simple Phobia. Archives of General Psychiatry, 49: 273–281.

Kendler, K. S., Neale, M. C., Kessler, R. C., Heath, A. C. & Eaves, L. J. (1993a). Major depression and phobias: the genetic and environmental sources of comorbidity. Psychological Medicine, 23: 361–371.

Kendler, K. S., Neale, M. C., Kessler, R. C., Heath, A. C. & Eaves, L. J. (1993b). A test of the equal environment assumption in twin studies of psychiatric illness. Behaviour Genetics, 23: 21–27.

Kendler, K. S., Walters, E. E., Neale, M. C., Kessler, R. C., Heath, A. C. & Eaves, L.J. (1995). The structure of the genetic and environmental risk factors for six major psychiatric disorders in women. Phobia, generalized anxiety disorder, panic disorder, bulimia, major depression, and alcoholism. Archives of General Psychiatry, 52: 374–383.

Kendler, K. S., Karkowski, L. M. & Prescott, C. A. (1999). Fears and phobias: reliability and heritability. Psychological Medicine, 29: 539–553.

Kendler, K. S., Myers, J., Prescott, C. A. & Neale, M. C. (2001). The genetic epidemiology of irrational fears and phobias in men. Archives of General Psychiatry, 58: 257–265.

Kendler, K. S., Jacobson, K. C., Myers, J. & Prescott, C. A. (2002). Sex differences in genetic and environmental risk factors for irrational fears and phobias. Psychological Medicine, 32: 209–217.

Kendler, K. S., Prescott, C. A., Myers, J. & Neale, M. C. (2003). The structure of genetic and environmental risk factors for common psychiatric and substance use disorders in men and women. Archives of General Psychiatry, 60: 929–937.

Kendler, K. S., Gardner, C. O., Annas, P., Neale, M. C., Eaves, L. J. & Lichtenstein, P. (2008). A longitudinal twin study of fears from middle childhood to early adulthood: evidence for a developmentally dynamic genome. Archives of General Psychiatry, 65: 421–429.

Kendler, K. S., Gardner, C. O., Annas, P. & Lichtenstein, P. (2008). The development of fears from early adolescence to young adulthood: a multivariate study. Psychological Medicine, 38: 1759–1769.

King, N. J., Gullone, E. & Ollendick, T. H. (1998). Etiology of childhood phobias: current status of Rachman's three pathways theory. Behaviour Research and Therapy, 36: 297–309.

LeBeau, R. T., Glenn, D., Liao, B., Wittchen, H. U., Beesdo-Baum, K., Ollendick, T., et al.(2010). Specific phobia: a review of DSM-IV specific phobia and preliminary recommendations for DSM-V. Depression and Anxiety, 27: 148–167.

Li, M. D., Cheng, R., Ma, J. Z. & Swan, G. E. (2003). A meta-analysis of estimated genetic and environmental effects on smoking behavior in male and female adult twins. Addiction, 98: 23–31.

LoBue, V., Rakinson, D. H. & DeLoache, J. S. (2010). Threat perception across the lifespan: evidence for multiple converging pathways. Current Directions in Psychological Science, 19: 375–379.

Lipsitz, J. D., Fyer, A. J., Paterniti, A. & Klein, D. F. (2001). Emetophobia: preliminary results of an internet survey. Depression and Anxiety, 14: 149–152.

Magee, W. J., Eaton, W. W., Wittchen, H. U., McGonagle, K. A. & Kessler, R. C. (1996). Agoraphobia, simple phobia, and social phobia in the National Comorbidity Survey. Archives of General Psychiatry, 53: 159–168.

Marks, I. M. & Mathews, A. M. (1979). Brief standard self-rating for phobic patients. Behavior Research and Therapy, 17: 263–267.

McNally, R. J. (1994). Choking phobia: a review of the literature. Comprehensive Psychiatry, 35: 83–89.

Menzies, R. G. & Clarke, J. C. (1993). The etiology of childhood water phobia. Behaviour Research and Therapy, 31: 499–501.

Menzies, R. G. & Clarke, J. C. (1995). The etiology of phobias: a non-associative account. Clinical Psychology Review, 15: 23–48.

Menzies, R. G., Kirkby, K. & Harris, L. M. (1998). The convergent validity of the phobia origins questionnaire (POQ): a review of the evidence. Behaviour Research and Therapy, 36: 1081–1089.

Middeldorp, C. M., Cath, D. C., Van Dyck, R. & Boomsma, D. I. (2005). The co-morbidity of anxiety and depression in the perspective of genetic epidemiology. A review of twin and family studies. Psychological Medicine, 35: 611–624.

Monroe, S. M. & Simons, A. D. (1991). Diathesis-stress theories in the context of life-stress research: implications for the depressive disorders. Psychological Bulletin, 110: 406–425.

Neale, M. C., Walters, E. E., Eaves, L. J., Kessler, R. C., Heath, A. C. & Kendler, K. S. (1994). Genetics of blood–injury fears and phobias: a population-based twin study. American Journal of Medical Genetics, 54: 326–334.

Oosterink, F. M. D., De Jongh, A. & Aartman, I. H. A. (2008). What are people afraid of during dental treatment? Anxiety-provoking capacity of 67 stimuli characteristic of the dental setting. European Journal of Oral Sciences, 116: 44–51.

Oosterink, F. M. D., De Jongh, A. & Hoogstraten, J. (2009). Prevalence of dental fear and phobia relative to other fear and phobia subtypes. European Journal of Oral Sciences, 117: 135–143.

Oosterink, F. M. D., De Jongh, A. & Aartman, I. H. (2009). Negative events and their potential risk of precipitating pathological forms of dental anxiety. Journal of Anxiety disorders, 23: 451–457.

Page, A. C. & Martin, N. G. (1998). Testing a genetic structure of blood–injury–injection fears. American Journal of Medical Genetics, 81: 377–384.

Poulton, R. & Menzies, R. G. (2002). Non-associative fear acquisition: a review of the evidence from retrospective and longitudinal research. Behaviour Researchand Therapy, 40: 127–149.

Rachman, S. (1977). The conditioning theory of fear-acquisition: a critical examination. Behaviour Research and Therapy, 15: 375–387.

Robins, L. N., Helzer, J. E., Weissman, M. M., Orvaschel, H., Gruenberg, E., Burke, J. D., et al. (1984). Lifetime prevalence of specific psychiatric disorders in three sites. Archives of General Psychiatry, 41: 949–958.

Robins, L. N., Wing, J., Wittchen, H. U., Helzer, J. E., Babor, T. F., Burke, J., et al. (1988).The composite international diagnostic interview. An epidemiologic instrument suitable for use in conjunction with different diagnostic systems and in different cultures. Archives of General Psychiatry, 45: 1069–1077.

Skre, I., Onstad, S., Torgersen, S., Philos, D. R., Lygren, S. & Kringlen, E. (2000). The heritability of common phobic fear: a twin study of a clinical sample. Journal of Anxiety Disorders, 14: 549–562.

Stewart, S. E. & Pauls, D. L. (2010). The genetics of obsessive–compulsive disorder. Focus, 8: 350–357.

Sutton, A. J., Abrams, K. R., Jones, D. R., Sheldon, T. A. & Song, F. (2000). Methods for meta-analysis in medical research. New York: John Wiley & Sons, Inc.

Tambs, K., Czajkowsky, N., Røysamb, E., Neale, M. C., Reichborn-Kjennerud, T., Aggen,S. H., et al. (2009). Structure of genetic and environmental risk factors for dimensional representations of DSM-IV anxiety disorders. British Journal of Psychiatry, 195: 301–307.

Torgersen, S. (1979). The nature and origin of common phobic fears. British Journal of Psychiatry, 134: 343–351.

Trumpf, J., Margraf, J., Vriends, N., Meyer, A. H. & Becker, E. S. (2010). Specific phobia predicts psychopathology in young women. Social Psychiatry and Psychiatric Epidemiology, 45: 1161–1166.

Vassend, O., Røysamb, E. & Nielsen, C. S. (2011). Dental anxiety in relation to neuroticism and pain sensitivity. A twin study. Journal of Anxiety Disorders, 25: 302–308.

Verweij, K. J., Zietsch, B. P., Lynskey, M. T., Medland, S. E., Neale, M. C., Martin, N.G., et al. (2010). Genetic and environmental influences on cannabis use initiation and problematic use: a meta-analysis of twin studies. Addiction, 105: 417–430.

It is not that I’m afraid of the dental drill. I’m not even afraid that it hurts. I can’t stand the feeling of losing control during treatment. It reminds me of other experiences in my life, when I completely lost control.

CHAPTER 3

The factor structure of dental fear

C.M.H.H. van Houtem, A.J. van Wijk, D. I. Boomsma,
L. Ligthart, C.M. Visscher, A. de Jongh

Submitted

Introduction

Fear of the dental treatment is a relatively common fear in the general population. About 30%-40% of the adult population in Western Societies report moderate levels of dental fear (Halonen et al., 2014; Singer et al., 2012), while 5 to 15% indicate to suffer from high fear levels (Hill et al., 2013; Humphris & King, 2011; Nicolas et al., 2007; Schuller et al., 2003). High levels of dental fear are likely to induce avoidance behavior, thereby increasing the risk of negatively affecting individuals' oral health (Vermaire et al., 2008; Mehrstedt et al., 2007; Schuller et al., 2003; Cohen et al., 2000; Stouthard & Hoogstraten, 1990).

Although the term "dental fear" suggests an unidimensional construct, it, in fact, encompasses a broad constellation of fears of objects and situations within the dental setting (e.g., Oosterink et al., 2008; De Jongh et al., 1998). Bearing the above in mind, to optimize treatment success, specifying individuals according to their fears of objects and situations within the dental setting, and classifying them into distinct typologies (Milgrom et al., 1985), is important (De Jongh et al., 2011).

To this end, Milgrom proposed a classification system consisting of dentally fearful patients having (I) a simple conditioned fear of specific dental stimuli; (II) somatic reactions during dental treatment; (III) generalized anxiety states, or (IV) distrust of dental personnel (Milgrom et al., 1985; Locker et al., 1999). However, although the authors used their broad clinical experience to classify patients in particular fear categories, using a more sophisticated method or model, to empirically identify groups of patients with similar response patterns is warranted.

Until now, only two studies have attempted to determine the underlying structure of fear of stimuli pertaining to different objects and situations present in the dental setting using a statistical method. Oosterink and colleagues (Oosterink et al., 2008) performed an exploratory factor analysis on a set of 67 stimuli present in the dental setting using a sample of almost 1,000 individuals. They identified a two-factor solution, with the first factor being an invasive treatment-related stimuli factor, and the second being a non-invasive-treatment related factor. However, close inspection of the results suggested that the two factors were very general in nature, with only modest explained variance (51.4%). A possible explanation for this relatively low proportion of explained variance might be the small number of individuals in relation to the large amount of stimuli included in the analyses. Moreover, a number of items showed low factor loadings and/or low communalities.

Building on the work of Oosterink (Oosterink, De Jongh & Aartman, 2008), Wong and colleagues (Wong et al., 2015) conducted an exploratory (EFA) and confirmatory factor analyses (CFA), and performed these on 73 dental objects or situations. Their EFA revealed a seven-factor solution (i.e., dental check-up, injection, scale and drill, surgery, empathy, perceived lack of control, and clinic environment) explaining 71.3% of the variance. How-

ever, the sample was relatively homogeneous as it consisted of university students with average levels of dental anxiety and a narrow age range. Additionally, the use of statistical procedures that create optimized linear combinations of variables using a low sample size (i.e., 160 and 300 for the EFA and the CFA, respectively), in combination with a high number of items, have been found to yield problematic outcomes, as these increase the probability of errors, minimize the accuracy of population estimates, and reduce the generalizability of the results (Osborne & Costello, 2004).

Therefore, the purpose of current study was to develop a descriptive framework for the classification of dental fear by describing the multidimensional structure of a set of common stimuli present in the dental setting using a large sample with a broad age range and diversity in level of education. This was done using exploratory factor analysis (EFA), whereas a second, independent sample was used to confirm the newly derived model by means of confirmatory factor analysis (CFA).

Material and Methods

Data collection and participants

Participants were members of twin families (i.e., twins and their relatives) registered with the Netherlands Twin Register (NTR, (18). Participants with an age ≥18 years (n = 27, 892) received an invitation to participate in a study on lifestyle and personality. Of them, 11,771 individuals (42.2%) completed the relevant questions in an online or offline version of the questionnaire (see for a detailed description of the sample and data collection van Houtem *et al.* (van Houtem et al., 2015) and Ligthart *et al.* (Ligthart et al., 2014).

Measures

Sociodemographic variables. The survey included questions regarding age and sex. Based on previous questionnaires (Willemsen et al., 2013) information regarding country of birth (i.e., The Netherlands *vs.* other country of birth) was available for 10,781 participants (91.6%), as well as information about the level of education (i.e., primary-low *vs.* intermediate-high), which was available for 8,500 individuals (72.2%).

Dental trait anxiety. Severity of dental trait anxiety was assessed using the Dental Anxiety Scale (DAS, (Corah, 1969). Responses to a total of 4 questions are scored from 1 to 5, resulting in total scores ranging from 4 (not anxious at all) to 20 (extremely anxious). DAS scores of 13 or higher are indicative of a high level of dental fear (Corah et al., 1978).

Fear of stimuli comprising the dental setting. To assess the fear of objects and situations related to the dental setting a set of 28 potentially fear-provoking stimuli present in the dental setting were used. These consisted of the most frequently feared stimuli from the set of 67 used in our previous study (Oosterink, De Jongh & Aartman, 2008), supplemented with three more physically related and clinically meaningful stimuli (i.e. the sense of gagging, vomiting and fainting) not used in previous studies. For the complete set of stimuli we refer to van Houtem et al. (van Houtem et al., 2015). The fear provoking nature of each stimulus was scored on a four-point scale, from 1 ('not at all fear provoking ') to 4 ('extremely fear provoking').

Statistical analyses

Descriptive statistics were obtained using IBM SPSS Statistics Version 20 (IBM Corp, Armonk, NY). The χ^2-test was used to analyze associations between categorical variables, the independent-samples t-test was used to compare groups on continuous variables. In order to explore the underlying structure of the most prevalent fears related to the dental treatment, an exploratory factor analysis (PCA) was performed on a random half of the sample. Factors with eigenvalues > 1 were extracted and Varimax rotation was performed to increase interpretability of the factor solutions. In order to derive a stable factor structure, the following stepwise procedure was followed. First, factor analysis was performed on the entire set of items. Factor loadings in the rotated component matrix were examined. An item with either a primary factor loading (i.e., the highest factor loading on a given factor) below .50, or an ambiguous item (a difference of less than .20 between the highest factor loading and the factor loading on a different factor) was deleted from the set of items. Next, a factor analysis was performed on the remaining set of items. This procedure was repeated until all items were non-ambiguous and showed a strong primary factor loading on one factor. Subsequently, factors were interpreted by looking at the content of the items with the highest factor loading on the respective factor. This factor structure was then fitted to the data on the other random half of the sample using confirmatory factor analysis (CFA) performed with IBM SPSS AMOS 22. Model fit was evaluated using the traditional χ^2-statistic with df and p-value, the RMSEA (<0.07), SRMS (<0.08), CFI (>0.95) and GFI (>0.95) (24). For all statistical analyses, a *p*-value <0.05 was considered statistically significant.

Results

Socio-demographic characteristics and dental anxiety

Table 1 presents data on the socio-demographic characteristics of the entire sample (n = 11,771 individuals). Of the participants 61.8% (n = 7,260) was female. Women had a sig-

Table 1. Socio-demographic characteristics and mean level of dental trait anxiety of the entire sample

	N	Proportion	Mean	*P-value*
Gender	11,771			
Male	4,501	38.2%	-	-
Female	7,270	61.8%	-	
Mean age (±SD)	11,771	-	44.38 (15.67)	
Male	4,576	-	46.44 (16.13)	< 0.001
Female	7,366	-	43.37 (15.36)	
Country of birth	10,781			
The Netherlands	10,556	97.9%	-	-
Any other country	225	2.1%	-	
Level of education	8,500			
primary-low	1,729	20.3%	-	-
intermediate-high	6,771	79.7%	-	
Mean level of dental anxiety (4-20; ±SD)	11,572	-	7.46 (2.73)	
Male	4,420	-	6.76 (2.31)	< 0.001
Female	7,152	-	7.90 (2.88)	

nificantly lower mean age than men ($p < 0.001$). Most of the participants were born in the Netherlands (97.9%) and had an intermediate or high level of education (79.7%). Women showed significantly higher mean levels of dental trait anxiety than men ($p < 0.001$).

The samples

The entire sample was randomly divided into two subsamples. The first sample consisted of 5,920 individuals, and the second sample consisted of 5,851 individuals. Firstly, the socio-demographic distributions of the two subsamples were compared. It appeared that the samples differed on gender ($\chi^2(1) = 4.30$; $p = 0.038$), i.e. the first subsample consisted of 37.3% males versus 39.2% in the second subsample. However, this difference was relatively small, but obviously significant as a result of the large sample size. Accordingly, no further action was undertaken. For the fear provoking stimuli "dentist drilling your tooth or molar" ($p = 0.016$), and "the sound of the drill" ($p = 0.032$) significantly higher mean scores were observed among the individuals of the first subsample. The two subsamples did not differ on any of the other variables, including the remaining 26 of the stimuli comprising the dental setting.

Exploratory factor analyses on the severity ratings of the fear provoking stimuli

Exploratory factor analysis was performed on the set of responses to the 28 fear provoking stimuli from a random half of the sample (subsample 1). The Kaiser-Meyer-Olkin measure of sampling adequacy was 0.97. The Bartlett's test of sphericity was significant ($p<0.001$), indicating that the data were suitable for factor analysis. The initial solution of the exploratory factor analyses revealed four factors with an eigenvalue >1, explaining 64% of the variance. Next, the stepwise procedure was followed until all items had a primary factor loading of >.50, and the second loading of at least .20 less than the primary factor loading. The final solution yielded a three-factor solution with 70.7% explained variance (see Table 2 for the rotated factor solution). When looking at the content of the items for each factor, the following interpretation was made: (1) an invasive-treatment-related factor; (2) a factor associated with lack of self-control; and (3) a factor associated with physical (internal) sensations.

Given this study was conducted among twin family members we tested the possible presence of some degree of dependency between the observations by repeating the EFA in a subsample comprising a random selection of only one person per family (n = 5,246). This analysis gave identical results compared with the EFA conducted in the original sample, with a three factor solution with 70.1% explained variance and the same items loading on each factor.

Table 2.Final rotated factor solution for the 3-factor model

Item	Factor loadings *			Communalities
4 Having surgery	.75			.67
5 Dentist drilling a tooth or molar	.76			.73
8 Extractions of tooth or molar	.81			.74
18 Having a root canal treatment	.79			.74
21 Cutting or tearing in soft tissue	.74			.69
23 Pain	.70			.63
25 Insufficient aneasthetics	.65			.67
3 Lying in the dental chair (position)		.68		.51
6 Not knowing what's happening in the mouth		.75		.73
12 The fact that you don't know what is going to happen	.40	.74		.73
15 Objects in the mouth		.66		.63
16 Lack of explanation by the dentist		.67		.65
17 Feeling helpless		.67		.67
26 Gagging			.87	.86
27 The sense of vomiting			.89	.90
28 Fainting			.81	.76

* FL < .40 are not displayed

Confirmatory factor analyses (CFA) on the severity ratings of the fear provoking stimuli

Using the individuals of the second subsample, a CFA was performed to fit the 3-factor structure model to the data. Statistics concerning model fit are reported in Table 3. The first model did show an acceptable fit to the data. Fit indices in general were just below the

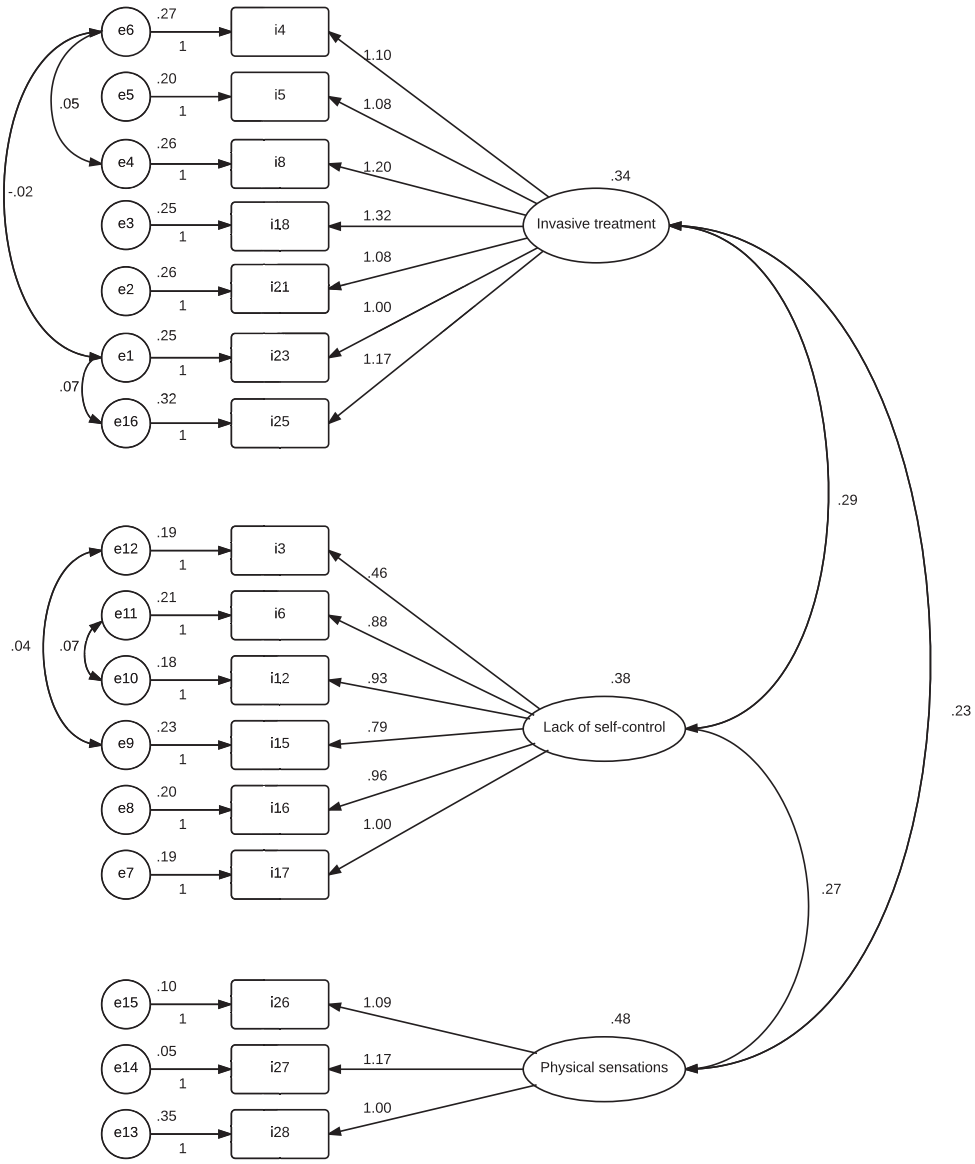

Figure 1. Factor structure of the CFA model

Table 3. Confirmatory factor analyses (CFA) on the severity ratings of the fear provoking stimuli

Model	RMR	GFI	CFI	RMSEA
3-factor	0.30	0.913	0.943	0.081
3-factor adjusted	0.029	0.941	0.961	0.069

criteria for a good fit. Inspection of the modifications indices showed that the model could be improved by correlating a number of error terms. The following items were considered to be comparable in content and were therefore allowed to correlate: (1) "undergoing a surgical operation" (item 4) and "having a tooth or molar extracted" (item 8); (2) "feeling pain" (item 23) and "insufficient anesthesia" (item 25); (3) "undergoing a surgical operation" (item 4) and "feeling pain" (item 23); (4) "lying back in the chair" (item 3) and "objects in the mouth" (item 15); and (5) "not knowing what is happening" (item 12) and "not knowing what is happening in your mouth" (item 6). These modifications led to a slight improvement of model fit (see Table 3). Overall, the model showed acceptable fit to the data. Therefore, the 3-factor structure underlying these data can be considered stable. Figure 1 shows the factor structure of the CFA model.

Discussion

The results of the present study, using a sufficiently large sample with a broad age range, showed a factor structure reflecting three different constructs underlying dental fear (i.e., "fear of invasive treatment", "lack of self-control", and "physical sensations"), together explaining about 70 percent of the variance of in total 28 anxiety provoking stimuli. Of these, 25 were rated as most prevalent in a previous study (Oosterink et al., 2008), while three clinically meaningful items were added for the purpose of the present study. The CFA carried out on the data of the second sample resulted in an acceptable fit for the two models that were examined. This suggests that the three-factor structure that was identified as underlying our data is stable, thereby supporting the notion that fears related to the dental treatment have a heterogeneous rather than an unidimensional nature (Oosterink, De Jongh & Aartman, 2008).

At first glance, the three factors identified seem at odds with those described by Wong et al. (2015) who identified seven factors, and Oosterink et al. (Oosterink et al., 2008) who found only two independent factors. Some of these differences can probably best be explained by variation in the description of the items included in the factor analyses, the cut-off point of the factor loadings and cross-loadings, the subjective interpretation of the results, and the relatively small sample sizes in relation to the large amount of stimuli which could have incurred relative limitations on the statistical power to detect the presence of

other, overall or independent factors of smaller magnitude. The items that loaded on the third factor of our model (i.e., "physical sensations"), relate to typical internal (i.e., bodily) sensations, were all added for the purpose of the present study, and had never before been part of any of the previous studies (Oosterink et al., 2008; Wong et al., 2015). However, there are a number of clear similarities between our framework and the previous ones. For example, both earlier studies identified factors related to invasive treatments. More specifically, the items that loaded on the "injection", "scale and drill" and "surgery" factor, identified by Wong et al. (2015), and most of the items used by Oosterink et al., (2008) that loaded on their "invasive treatment-related stimuli factor" can be subsumed under our "fear of invasive treatment factor". Similarly, Wong's et al. (2015) "lack of control-factor" corresponds by and large with the "lack of self-control" factor of our model.

A descriptive framework for the classification of dental fear categories may be important as this might contribute to the development of new questionnaires for assessing dental fear subtypes. Currently, most questionnaires for the assessment of dental fear and dental anxiety include only a small set (4-15) of potentially anxiety provoking stimuli (e.g., the IDAF-4C+ (Armfield, 2010); Dental Anxiety Scale (Corah, 1969); the MDAS (Humphris et al., 1995); the S-DAI (Aartman, 1998); and the Dental Fear Survey (Kleinknecht et al., 1984)) which do not fully cover all fears present in the dental setting (see Oosterink (Oosterink et al., De Jongh & Aartman, 2008)), but also fail to provide enough information about the specific stimuli the individual patient fears.

The validity of the three-factor structure is further supported by the fact that this model seems to almost perfectly relate to the three distinct types of treatment strategies that are already applied to various subgroups of dental patients to tailor a specific treatment to patients' individual problems in clinical practice. For example, as to the first factor in our model, for fear of invasive treatment (with stimuli as "dentist drilling a tooth or molar"' or "having a root canal treatment") there is one primary, evidence-based treatment and that is *in vivo* exposure to patients' anxiety provoking stimuli (Armfield & Eaton, 2013; De Jongh et al., 2005). For lack of self-control, the second factor in our model (with stimuli like "not knowing what is going to happen" or "feeling helpless"), it is generally recommended to provide a sense of control and to heighten predictability during treatment, for instance by offering the patient the ability to use a stop signal, in order to initiate a break during treatment, and to provide the patient with information about the dental procedure which help correct misconceptions about dental treatment (Armfield & Eaton, 2013; De Jongh et al., 2005). For the third factor in our model, the experience of physical sensations which are related to, for example, "fainting" or "gagging", it is recommended to focus treatment on reducing these bodily sensations (De Jongh et al., 2005). For instance, the evidence based approach to prevent fainting in response to a confrontation to blood or injury during dental treatment is "applied tension" which consists of tensing all muscles to increase blood pres-

sure (Ayala et al., 2009; Öst et al., 1991). Hence, each factor in our newly derived model reflects a distinct type of fear related to dental treatment, requiring a specific intervention to treat that particular condition. To this end, the three-factor structure model may facilitate guiding oral health professionals in appropriate decision-making about tailoring particular interventions to individual patients.

Given the heterogeneity of the dental fears as supported by the factor structure, the present findings support the notion that the constructs as indicated by the terms "dental fear" or "dental phobia" alone are not tenable designations to classify individuals with fear of the dental setting (see also De Jongh et al., 2011; Oosterink et al., 2008; De Jongh et al., 2005; Milgrom et al., 1997; De Jongh et al., 1995) as these fail to account for the broad spectrum of fear evoking objects and situations present within the dental setting. Therefore, the present findings may be helpful to develop a new descriptive framework for the classification of dental fear by making distinctions among the various fear typologies, rather than by using the global term 'dental fear' or 'dental phobia' *per se*.

A few limitations need to be mentioned here. Given that participants were asked to rate the fear provoking nature of the stimuli, it is conceivable that a part of the participants had never been exposed to at least some of the objects or situations as presented in the questionnaire prior to the study. This could have resulted in either an overestimation or underestimation of the fear provoking nature of particular stimuli. Finally, since we included only 28 stimuli in our analyses, we cannot rule out the possibility that still other factors are underlying the construct of dental fear.

In conclusion, the present findings suggest that dental fear should best be considered a heterogeneous fear reflected by at least three separated factors: fear of invasive treatment, lack of self-control and the experience of physical sensations. This classification in distinct fear typologies may improve our understanding of the nature of dental fear, and might encourage the development of new measures to better guide clinicians in choosing appropriate fear reducing interventions for individual patients.

References

Aartman, I. H. A. (1998). Reliability & validity of the short version of the Dental Anxiety Inventory. Community Dentistry and Oral Epidemiology, 26: 350–354.

Armfield, J. & Heaton, L. (2013). Management of fear and anxiety in the dental clinic: a review. Australian Dental Journal, 58: 390–407.

Ayala, E.S., Meuret, A.E. & Ritz, T. (2009). Treatments for blood-injury-injection phobia: a critical review of current evidence. Journal of Psychiatric Research, 43: 1235–1242.

Armfield, J.M. (2010). Development and psychometric evaluation of the Index of Dental Anxiety and Fear (IDAF-4C+). Psychological Assessment, 22: 279–287.

Cohen, S.M., Fiske, J. & Newton, J.T. (2000).The impact of dental anxiety on daily living. British Dental Journal, 189: 385-90.

Corah, N.L. (1969). Development of a dental anxiety scale. Journal of Dental Research, 48: 596.

Corah, N.L., Gale, E.N. & Illig, S.J. (1978). Assessment of a dental anxiety scale. The Journal of the American Dental Association, 97: 816–819.

De Jongh, A., Bongaarts, G., Vermeule, I., Visser, K., De Vos, P. & Makkes, P. (1998). Blood-injury-injection phobia and dental phobia. Behaviour Research and Therapy, 36: 971-82.

De Jongh, A., Oosterink, F.M.D., Kieffer, J.M., Hoogstraten, J. & Aartman, I.H.A. (2011). The Structure of Common Fears: Comparing Three Different Models. The American Journal of Psychology, 124: 141-149.

De Jongh, A., Muris, P., ter Horst, G., Duyx, M.P. (1995). Acquisition and maintenance of dental anxiety: the role of conditioning experiences and cognitive factors. Behaviour Research and Therapy, 33: 205–210.

De Jongh, A., Adair, P. & Meijerink-Anderson, M. (2005). Clinical management of dental anxiety: what works for whom? International Dental Journal, 55: 73–80.

Halonen H., Salo T., Hakko, H. & Räsänen P. (2014). The association between dental anxiety, general clinical anxiety and depression among Finnish university students. Oral Health and DentalManagement, 13: 320-325.

Hill, K.B., Chadwick, B., Freeman, R., O'Sullivan, I. & Murray, J.J. (2013). Adult Dental Health Survey 2009: relationships between dental attendance patterns, oral health behaviour and the current barriers to dental care. British Dental Journal, 214: 25-32.

Hooper, D., Coughlan, J., Mullen, M. (2008). Structural Equation Modelling: Guidelines for Determining Model Fit. Electronic Journal of Business Research Methods, 6: 53-6025.

Houtem, C. M. H. H. van, van Wijk, A. J., Boomsma, D. I., Ligthart, L., Visscher, C. M. & De Jongh, A. (2015), Self-reported gagging in dentistry: prevalence, psycho-social correlates and oral health. Journal of Oral Rehabilitation, 42: 487–494.

Houtem, C.M.H.H. van, Aartman, I.H.A., Boomsma, D.I., Ligthart, L., Visscher, C.M. & De Jongh, A. (2014). Is dental phobia a blood-injection-injury phobia? Depression and Anxiety, 31: 1026–1034.

Humphris, G.M., Morrison, T. & Lindsay, S.J.E. (1995). The Modified Dental Anxiety Scale: Validation and United Kingdom Norms. Community Dental Health, 12: 143-150.

Humphris, G. & King, K. (2011). The prevalence of dental anxiety across previous distressing experiences. Journal of Anxiety Disorders, 25: 232-236.

Kleinknecht, R. A., Thorndike, R. M., McGlynn, F. D. & Harkavy, J. (1984). Factor analysis of the dental fear survey with cross-validation. Journal of the American Dental Association (1939), 108: 59-61.

Ligthart, L., Visscher, C.M., van Houtem, C.M.H.H., Geels, L.M., Vink, J.M., De Jongh, A. & Boomsma, D.I. (2014). Pain symptoms in a Dutch population sample: relationship with sex, age and anxious depression. The Journal of Pain, 15: 945-955.

Locker, D., Liddell, A. & Shapiro, D. (1999). Diagnostic categories of dental anxiety: a population-based study. Behaviour Research and Therapy, 37: 25-37.

Mehrstedt, M., John, M.T., Tönnies, S. & Micheelis, W. (2007). Oral health-related quality of life in patients with dental anxiety. Community Dentistry and Oral Epidemiology, 35: 357-63.

Milgrom, P., Weinstein, P., Kleinknecht, R. & Getz, T. (1985). Treating Fearful Dental Patients. Reston, VA: Reston Publishing Co.

Milgrom, P., Coldwell, S.E., Getz, T., Weinstein, P., Ramsay, D.S. (1997). Four dimensions of fear of dental injections. Journal of the American Dental Association (1939), 128: 756-766.

Nicolas, E., Collado, V., Faulks, D., Bullier, B. & Hennequin, M. (2007). A national cross-sectional survey of dental anxiety in the French adult population. BMC Oral Health, 7: 12.

Oosterink, F. M.D., De Jongh, A. & Aartman, I.H.A. (2008). What are people afraid of during dental treatment? Anxiety-provoking capacity of 67 stimuli characteristic of the dental setting. European Journal of Oral Sciences, 116: 44–51.

Osborne, J.W. & Costello, A.B. (2004). Sample size and subject to item ratio in principal components analysis. Practical Assessment, Research & Evaluation, 9(11).

Öst, L.G., Fellenius, J. & Sterner U. (1991). Applied tension, exposure in vivo, and tension-only in the treatment of blood phobia. Behaviour Research and Therapy, 29: 561–574.

Schuller, A.A., Willumsen, T. & Holst, D. (2003). Are there differences in oral health and oral health behavior between individuals with high and low dental fear? Community Dentistry and Oral Epidemiology, 31: 116-121.

Singer, R., Cardenas, G., Xavier, J., Jeanty, Y., Pereyra, M., Rodriguez, A. & Metsch, L.R. (2012). Dental anxiety and the use of oral health services among people attending two HIV primary care clinics in Miami. Public Health Reports; 127 Suppl 2: 36-44.

Stouthard, M. E. A. & Hoogstraten, J. (1990). Prevalence of dental anxiety in the Netherlands. Community Dentistry and Oral Epidemiology, 18: 139–142.

Vermaire, J.H., De Jongh, A. & Aartman I.H. (2008). Dental anxiety and quality of life: the effect of dental treatment. Community Dentistry and Oral Epidemiology, 36: 409-16

Willemsen, G., Vink, J.M., Abdellaoui, A., den Braber, A., van Beek, J.H.D.A., Draisma, H.H.M. et al. (2013). The Adult Netherlands Twin Register: Twenty-Five Years of Survey and Biological Data Collection. Twin Research and Human Genetics, 16: 271–281.

Wong, H.M., Mak, C.M. & To,W.M. (2015). Development of a Dental Anxiety Provoking Scale: A pilot study in Hong Kong. Journal of Dental Sciences, 10: 240-247.

Until today, I have avoided to visit a dentist for almost sixty years. When I was seven years old the dentist gave me an extremely painful injection. Then he extracted my molar, although the anesthesia didn't work properly. The dentist didn't believe me. After all these years, his angry face still comes to my mind and makes me anxious again.

CHAPTER 4

Presence, content and characteristics of memories of individuals with dental phobia

C.M.H.H. van Houtem, A.J. van Wijk, A. de Jongh

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Introduction

Enhanced memory of emotional events is a well-known phenomenon (De Quervain et al., 2009). Intrusive, involuntary memories of an aversive or distressing event, whereby the specific content of the memory corresponds with that of the event, are among the key features of posttraumatic stress disorder (PTSD; American Psychiatric Association, 2000; Holmes et al., 2005). These memories involve a range of sensory modalities, albeit visual aspects are most commonly reported (e.g., Ehlers et al., 2002; Engelhard et al., 2002), and include characteristics such as vividness, intrusiveness, and the sense that the event seems to be happening again in the present (Michael et al., 2005). Some of these characteristics have been found to be associated with disturbance and emotion (Arntz et al., 2005; Michael et al., 2005), as well as symptom severity (Whitaker et al., 2008; Rubin et al., 2004; Berntsen et al., 2003; Willert & Rubin, 2003).

In recent years, a number of studies have shown that intrusive mental imagery is not unique for PTSD *per se* and also occurs in other psychiatric disorders (Hagenaars & Holmes, 2012), including anxiety disorders such as social phobia (Hackmann et al., 2000; Hackmann et al., 1998), agoraphobia (Day et al., 2004), obsessive compulsive disorder (Clark & Rhyno, 2005), and health anxiety (Muse et al., 2010).

Despite the fact that theories regarding phobia onset predict that disproportionate anxiety results from exposure to negative, disturbing life events (Davey, 1997), a surprisingly limited number of studies have been conducted to study the relationship between aversive memories and the presence of fears or specific phobias. One of the exceptions is a study on spider phobia in which the participants were asked whether they had experienced intrusive spider images and whether there was a specific early memory closely linked to that image (Pratt et al., 2004). The majority of individuals in the spider-anxious group, but none of a control group, reported spontaneous, recurrent images associated with their fear of spiders. About half of the participants (55%) reported that their images were associated with an early memory. A study among individuals with and without emetophobia found that significantly more phobic individuals could recall at least one memory of their own vomiting compared with the control group without emetophobia (Veale et al., 2013). Moreover, they rated the memories of their own vomiting experiences as significantly more distressing than individuals in the control group. Thus, it seems that in specific phobias, memories of distressing events play a significant role.

A substantial part of the existing studies regarding memories of individuals suffering from a specific phobia has been conducted in the area of dental phobia and dental fear. It has been found that dentally anxious individuals are likely to report a disturbing dental experience (Moore et al., 1991) and suffer from significantly more symptoms of re-experiencing, insomnia, and avoidance of reminders of past dental events than their moderately anxious

counterparts (De Jongh et al., 2003; De Jongh et al., 2006; De Jongh et al., 2002). For instance, in one study among individuals with high levels of dental anxiety, it was found that 43.3% indicated that they suffered from intrusive re-experiencing of past events when anticipating dental treatment (De Jongh et al., 2006). Thus, memories of past aversive events seem to be common features in dental fear and phobia. However, knowledge about the content and characteristics of specific memories is limited. Also, the possible role of these features in the development, exacerbation, and maintenance of dental fear and dental phobia, as well as the possible association between the characteristics of these memories and current levels of individuals' dental trait anxiety, is generally unclear.

Therefore, the first aim of the present study was to assess the presence, content, and characteristics (i.e., vividness, disturbance, and sense of reliving) of memories of events that initiated or exacerbated dental trait anxiety levels of individuals with dental phobia (n = 42). The results were compared with two reference groups, that is, individuals with (1) a high level of dental trait anxiety, but not fulfilling the *Diagnostic and Statistical Manual of Mental Disorders, 4th edition* (DSM-IV) criteria of dental phobia ('subthreshold dental phobia'; n = 41), and (2) a normal level of dental trait anxiety ('normal controls'; n = 70). It was hypothesized that a significantly higher proportion of the dental phobic patients would report disturbing core memories relative to the normal controls and based on PTSD research, that their memories would have a greater emotional intensity, intrusiveness, and avoidance propensity. Based upon the literature, it is not clear whether or not patients who are dentally anxious, but do not meet the threshold of dental phobia, would differ from both groups in terms of their memory characteristics. Therefore, examining these possible differences was also an aim of the present study, but was exploratory in nature.

The third aim of the present study was to determine the relationship between patients' severity of dental trait anxiety and some key features of these memories. It was predicted that greater severity of dental trait anxiety was positively associated with higher emotional intensity, intrusiveness, and avoidance propensity of the disturbing core memory.

Method

Participants

Three groups of participants were included in the current study: (1) phobic patients visiting a special dental fear clinic in Amsterdam, the Netherlands (further referred to as 'dental phobics'); (2) subthreshold phobic patients visiting this dental fear clinic (further referred to as 'subthreshold dental phobics'); and (3) patients of a general dental practice in the Netherlands with normal levels of dental trait anxiety (further referred to as 'normal controls'). In order to apply for treatment at the dental fear clinic, patients needed to fulfill

strict criteria such as a minimal score on several dental anxiety questionnaires, evidence of severe avoidance behavior in the past, or being difficult or impossible to treat by a dentist in a general dental practice.

Measures

Materials

Dental trait anxiety was indexed using the Dental Anxiety Scale (DAS; Corah, 1969). This four-item measuring scale is the questionnaire most widely used in studies of dental anxiety (Corah, Gale & Illig, 1978). Responses are scored from 1 to 5, providing total scores ranging from 4 (not anxious at all) to 20 (extremely anxious). DAS scores of 13 or higher are considered indicative of high dental trait anxiety. The test–retest reliability of the DAS showed an intraclass correlation of 0.82 (Corah, 1969). Cronbach's alpha in the current study was 0.69 for phobics, 0.83 for subthreshold phobics, and 0.80 for controls (overall $\alpha = 0.96$).

The level of exposure to distressing (dental) events was assessed using the Level of Exposure–Dental Experiences Questionnaire (LOE-DEQ), a self-report checklist inquiring about potentially overwhelming events in the individual's past (Oosterink et al., 2008). The LOE-DEQ had a satisfactory test–retest reliability (intraclass correlation coefficient = 0.78; Oosterink et al., 2008). The format of this inventory allows for calculating scores for the presence of separate trauma areas with respect to 21 typical dental and potentially traumatic experiences and eight general/other traumatic life events fulfilling the DSM-IV Text Revision (DSM-IV-TR) stressor criteria (e.g., a serious accident or being a victim of a violent crime). Dental experiences were dental procedures (e.g., a root canal treatment or an injection), behavior of the dentist or oral surgeon (e.g., a treatment by an impolite or rude dentist or being criticized by a dentist), patients' emotions during a dental treatment (e.g., embarrassment or helplessness), and negative dental events (e.g., witnessing a treatment of an extremely anxious dental patient). Participants are requested to indicate whether they had 'ever' (1) or 'never' (0) experienced any of these events. Items are scored and summed to give an overall frequency score ranging from 0 to 21 for dental experiences and 0 to 8 for general traumatic experiences.

The Phobia Checklist was used for the assessment of dental phobia (Oosterink, De Jongh & Hoogstraten, 2009). This screening tool was validated against the Structured Clinical Interview for DSM-IV (First & Gibbon, 2004) and has proven to be a valid instrument for the assessment of dental phobia (i.e., sensitivity = 0.95, specificity = 0.99, overall hit rate = 97%; Oosterink et al., 2009). The Phobia Checklist consists of four questions based on the DSM-IV-TR criteria (APA, 2000) for specific phobia. An individual is classified as a dental phobic only when all four questions of the Phobia Checklist are answered in the affirmative. In

the present study, an individual was classified as a subthreshold dental phobic when he or she had indicated a high level of dental trait anxiety as indexed by the DAS (Corah, 1969), and less than four questions of the Phobia Checklist were answered in the affirmative. An individual was classified as a normal control when he or she visited a dental practice, had normal levels of dental trait anxiety (i.e., a score of ≤12 on the DAS), and less than four questions of the Phobia Checklist were answered in the affirmative.

A semi-structured interview, the so called 'Full Intrusions Interview' adapted from Reynolds and Brewin (1999) was administered to identify whether the participants had memories of distressing events that initiated or exacerbated dental anxiety. Next, the characteristics of that memory were determined (i.e., the emotional intensity, intrusiveness, and avoidance propensity of that memory). Patients were asked to rate the emotional intensity (i.e., vividness, disturbance, and sense of reliving) of the memory on an 11-point Numeric Rating Scale. The Dutch version of the Impact of Event Scale (IES; Horowitz et al., 1979; Kleber et al., 1992) was used to index intrusiveness and avoidance propensity of this memory. Patients were explicitly instructed to fill out the IES related to this memory. The IES consists of 15 items constituting the subscales intrusions and avoidance. Adequate test–retest reliabilities were reported for the two subscales of the IES (0.87 for IES intrusion and 0.79 for IES avoidance; Horowitz et al., 1979). When scoring the IES, subjects are asked to indicate how frequently the symptoms were present during the past seven days. The frequency of each symptom is scored using a four-point response format, ranging from 'not at all' (0), 'rarely' (1), 'sometimes' (3) to 'often' (5). The scores can be summed to produce a total IES score (range 0–75), and two subscale scores for intrusion (range 0–35) and for avoidance (range 0–40) with a higher score indicating a greater level of intrusion (i.e., the loss of voluntary control over the regulation of thoughts) or avoidance (i.e., the extent to which memories are consciously suppressed). A score of 26 is considered the cut-off point for a clinically significant level of trauma-related symptomatology (Kleber et al., 1992). Cronbach's alpha for the current study for the IES intrusions scale was 0.89 for phobics, 0.87 for subthreshold phobics, and 0.86 for normal controls (overall $\alpha = 0.92$). For the avoidance scale, Cronbach's alpha was 0.79 for phobics, 0.87 for subthreshold phobics, and 0.90 for controls (overall $\alpha = 0.89$).

The independent variable in the current study was the group to which the subject belonged (i.e., dental phobics, subthreshold dental phobics, or normal controls). Dependent variables in the current study were gender, age, country of birth, level of dental trait anxiety, level of exposure to distressing (dental) events, and the emotional intensity, intrusiveness, and avoidance propensity of the memory.

Procedure

The study was based on a prospective design with two assessment points (T1 and T2; see Figure 1 for the flowchart) and was conducted between April 2010 and June 2012. Trained dental students invited patients of the dental fear clinic (*n* = 267, i.e., both dental phobics and subthreshold dental phobics) and patients of the general dental practice (i.e., the normal controls, *n* = 103) by telephone to participate in the study, and checked whether the patients fulfilled the inclusion criteria (i.e., age ≥ 18 years, good skills of the Dutch language, and no cognitive impairment) and were willing to participate (T0). Those who were willing to participate and fulfilled the inclusion criteria were sent a letter containing additional information and a request to fill out measures on severity of dental trait anxiety and the level of exposure to prior distressing (dental) events (T1). Of the participants, 140 patients of the dental fear clinic and 85 of the ordinary dental practice completed these measures. Patients of the general dental practice were excluded from the study if they were highly anxious (DAS

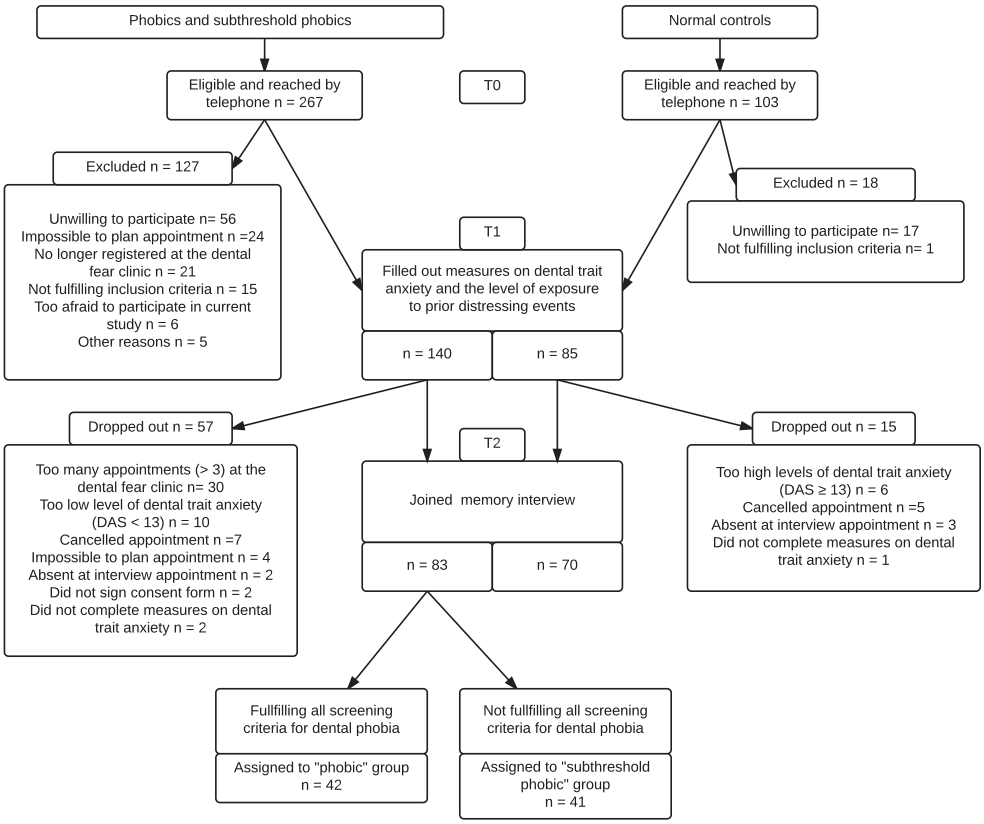

Figure 1. Flowchart

score ≥ 13) or met the criteria for dental phobia, in order to include a true sample of dentally high anxious cases with low anxious controls.

All groups of participants had to undergo both a structured and a semi-structured interview (T2) conducted by one researcher, Caroline van Houtem (CVH). Dental phobics and subthreshold dental phobics were interviewed prior to their third appointment, at the beginning of an anxiety reducing treatment program (for a description of the treatment, see Aartman et al., 2000). Normal controls were interviewed before an appointment at the general dental practice. During this interview, demographic data were collected (i.e., gender and country of birth). Next, the Phobia Checklist (Oosterink et al., 2009) was used to identify whether or not the diagnostic criteria of dental phobia (APA, 2000) were met. If so, patients were assigned to the dental phobic group (n = 42), or to a group with individuals not fulfilling all screening criteria for dental phobia (i.e., the subthreshold dental phobic group; n = 41; Figure 1). Then, a semi-structured interview (Reynolds & Brewin, 1999), lasting approximately 30 minutes, was conducted to investigate the presence, content, and characteristics of the memory of the event that, according to the patient, initiated or exacerbated his or her dental anxiety. For the purpose of the present study, memories had to consist of a specific scene that had actually happened, being a dental experience or another traumatic life event. The participants who were able to report more than one memory had to decide which memory was most closely related to the onset or aggravation of their dental anxiety. One dental phobic and one subthreshold dental phobic came late for the assessment procedure and, consequently, did not complete the assessment in time. Ethical approval for the study was granted by the local ethical committee (METc VU, protocol number 2007/262).

Results

General differences among groups

The descriptive statistics are displayed in Table 1. Although there was a trend showing a higher prevalence of women in the phobic and high anxious group, the groups did not differ significantly in terms of distribution of gender according to the chi-square test [χ^2 (2) = 5.52; p = 0.063]. No significant difference among groups was found in country of birth [χ^2 (2) = 0.88; p = 0.64], but one-way analysis of variance (ANOVA) showed that groups differed significantly in mean age [F (2, 149) = 3.97; p = 0.021]. Post-hoc analyses demonstrated that the normal controls had a significantly higher mean age than both other groups (p < 0.05). Results of two-way (groups by gender) ANOVA on dental trait anxiety showed that the groups differed significantly [F (2, 150) = 392.74; p < 0.001]. Post-hoc analyses showed that the normal controls had significantly lower levels of dental trait anxiety than the other groups (ps < 0.001). The difference in anxiety level was present in both men and women;

Table 1. Demographic variables, mean dental trait anxiety (DAS) and level of exposure to distressing events within and outside the dental setting (LOE-DEQ) in male and female dental phobics, subthreshold dental phobics and normal controls

	Dental phobic			**Subthreshold dental phobic**			**Normal control**				
	Proportion		**n**	**Proportion**		**n**	**Proportion**		**n**	***P***	η^2_p
Gender			42			41			70		
Male	31.0%		13	31.7%		13	50.0%		35	0.063	-
Female	69.0%		29	68.3%		28	50.0%		35		
Country of birth			42			40			70		
Dutch	90.5%		38	87.5%		35	92.9%		65	0.64	-
Other	9.5%		4	12.5%		5	7.1%		5		
	Mean	**± SD**	**n**	**Mean**	**± SD**	**n**	**Mean**	**± SD**	**n**	***P***	
Mean age in years	45.78	12.43	42	45.18	12.25	41	51.70	14.90	69	0.021	-
Male	43.55	10.98	13	44.81	12.51	13	53.42	11.45	35	0.034	-
Female	46.78	13.08	29	45.36	12.35	28	49.93	15.36	34	0.41	-
Mean DAS score (4-20)	17.71	2.17	42	16.88	2.56	41	7.31	1.98	70	<0.001	0.84
Male	17.08	2.40	13	16.77	3.00	13	7.09	2.01	35	<0.001	0.82
Female	18.00	2.04	29	16.93	2.39	28	7.54	1.96	35	<0.001	0.84
Within dental setting (0-21)	13.38	4.48	21	12.56	3.96	18	5.02	4.66	63	<0.001	0.43
Outside dental setting (0-8)	3.52	1.86	21	3.67	1.61	18	2.59	1.76	63	0.022	0.074

that is, no interaction between dental trait anxiety (groups) and gender was found [F (2, 147) = 0.28; $p = 0.76$]. Another set of two-way (groups by gender) ANOVAs on the level of exposure to distressing events (on the subscales within and outside the dental setting) showed that the groups differed significantly for events both within [F (2, 99) = 37.93; $p < 0.001$] and outside the dental setting [F (2, 99) = 3.98; $p = 0.022$]. Post-hoc analyses revealed that the normal controls reported significantly lower levels of exposure to distressing events on both subscales than both other groups ($ps < 0.05$). No interaction between individuals' level of exposure to distressing events inside the dental setting [F (2, 96) = 0.11; $p = 0.90$] and outside the dental setting [F (2, 96) = 0.24; $p = 0.79$], and gender was found.

Differences in memories among groups

Differences in presence of the memories

Of the dental phobic ($n = 41$) and subthreshold phobic ($n = 40$), individuals who completed the memory interview on T2 97.6% ($n = 40$) and 95.0% ($n = 38$), respectively, reported a memory of an aversive or distressing event that initiated or exacerbated their dental anxi-

ety. Both the proportion of phobic individuals and the proportion of subthreshold phobic individuals were significantly higher than the proportion of normal controls reporting a memory [72.9%, $n = 51$; χ^2 (2) = 14.76, p = 0.001; and χ^2 (2) = 15.00; $p < 0.001$ respectively]. The remaining phobics (n = 1) and subthreshold phobics (n = 2) reported memories of several traumatic events and were not able to select any specific memory related to the cause or exacerbation of their dental anxiety.

Differences in content of the memories

Memories were categorized in terms of content related to (1) the dental setting; and (2) another negative life event. See Table 2 for examples of memories that were reported. Significant differences were found regarding the content of the memory of the dental phobic and the control group, and between the subthreshold phobic and the control group. Compared with the normal controls reported both the dental phobics and the subthreshold dental phobics significantly more often to have a memory with a content related to a negative life event [χ^2(1) = 5.33; p = 0.021, and χ^2 (1) = 5.62; p = 0.018, respectively]. However, the majority of the memories of the phobic (90.0%; n = 36) and subthreshold phobics (89.5%; n = 34), and all the memories of the normal controls who reported such a memory (100%; n = 51) involved the dental setting.

Table 2. Examples of memories

Content	Examples
Dental setting	"As a child a molar was extracted while the anesthesia didn't work properly. It was extremely painful and the dentist ignored that."
	"A dentist visited my school. During the check-up I didn't want to open my mouth. The dentist put rings of steel on his fingers and pulls my jaws open.
	"I had a root canal treatment without local anesthesia. The dentist prohibited me to complain. I felt helpless."
Other negative life event	"My boyfriend committed suicide."
	"I received a wrong medical diagnosis."
	"An airplane crashed into my apartment."

Differences in memory characteristics

Time since event

Table 3 presents the data concerning the time span and characteristics (i.e., emotional intensity and PTSD symptom severity) of the memories of all groups. Using a one-way ANOVA, no significant difference was found between groups in the time that passed since the disturbing event described in the memory occurred [F (2, 123) = 0.48; p = 0.62].

Table 3. Memory characteristics in male and female dental phobics, subthreshold dental phobics and normal controls

	Dental phobic			Subthreshold dental phobic			Normal control				
Memory characteristics	**Mean**	**± SD**	**n**	**Mean**	**± SD**	**n**	**Mean**	**± SD**	**n**	***p***	η^2_p
Time span *(years ago)*	25.44	15.01	39	21.92	16.74	38	24.95	19.12	49	0.71	0.008
Emotional intensity											
Vividness (0-10)	7.13	2.20	39	7.37	2.27	38	4.08	2.99	49	<0.001	0.27
male	6.25	2.92	12	7.62	1.81	13	3.32	2.95	25	<0.001	
female	7.52	1.72	27	7.24	2.51	25	4.88	2.88	24	<0.001	
Disturbance (0-10)	7.72	2.70	39	7.87	2.58	38	4.02	3.25	49	<0.001	0.29
male	6.83	3.69	12	8.15	2.23	13	3.13	3.24	25	<00.01	
female	8.11	2.08	27	7.72	2.78	25	4.96	3.04	24	<0.001	
Sense of reliving (0-10)	5.67	3.18	39	4.74	3.18	38	1.59	2.03	49	<0.001	0.30
male	4.92	3.78	12	4.62	3.23	13	1.56	2.14	25	0.001	
female	6.00	2.89	27	4.80	3.22	25	1.63	1.95	24	<0.001	
Intrusiveness and avoidance tendency											
IES total (0-75)	32.04	19.41	37	26.91	18.95	33	5.67	10.38	51	<0.001	0.36
male	25.09	20.60	11	26.82	19.55	11	4.08	7.93	25	<0.001	
female	34.98	18.51	26	26.95	19.10	22	7.19	12.25	26	<0.001	
IES intrusion (0-35)	15.01	10.33	37	12.55	9.20	33	2.69	4.93	51	<0.001	0.33
male	10.27	10.85	11	12.09	10.19	11	1.84	3.57	25	0.001	
Female	17.02	9.62	26	12.77	8.90	22	3.50	5.91	26	<0.001	
IES avoidance (0-40)	17.03	10.26	37	14.36	10.54	33	2.98	5.87	51	<0.001	0.35
Male	14.82	11.42	11	14.73	10.01	11	2.24	5.04	25	<0.001	
female	17.96	9.81	26	14.18	11.03	22	3.69	6.60	26	<0.001	

Differences in emotional intensity of the memories

The three groups were compared regarding vividness, disturbance, and sense of reliving using a two-way (group by gender) ANOVA. The memories of the groups differed significantly in vividness, [F (2, 123) = 22.99; $p < 0.001$], disturbance [F (2, 123) = 25.48; $p < 0.001$] and sense of reliving [F (2, 123) = 26.26; $p < 0.001$]. Post-hoc analyses revealed that the memories of the normal controls had a significantly lower level of vividness, disturbance, and sense of reliving compared with the memories of both the dental phobic and the subthreshold phobic group (all *ps* < 0.001). No differences between the dental phobic and subthreshold dental phobic group were found. No interaction with gender was found for the scores on vividness [F (2, 121) = 1.43; $p = 0.24$], disturbance [F (2, 121) = 1.73; $p = 0.18$], and the sense of reliving [F (2, 121) = 0.34; $p = 0.71$] of the memories.

Differences in intrusiveness and avoidance tendency of the memories

The three groups were compared on IES total scores, intrusion, and avoidance scores using a two-way (group by gender) ANOVA. The groups differed significantly on IES total scores [F (2, 118) = 33.71; p = <0.001], on intrusion [F (2, 118) = 28.76; p = <0.001], and on avoidance scores [F (2, 118) = 32.22; p = <0.001]. Post-hoc analyses showed that normal controls had significantly lower levels of IES total scores and lower levels of intrusion and avoidance scores than both other groups (all *ps* < 0.001). For neither IES total score [F (2, 115) = 0.75; p = 0.47], nor intrusion [F (2, 115) = 1.33; p = 0.27], nor avoidance [F (2, 115) = 0.33; p = 0.72], an interaction with gender was found.

Relationship between dental trait anxiety and memory characteristics of the disturbing memory in anxious individuals and controls

Table 4 shows Pearson's correlation coefficients between dental trait anxiety and memory characteristics of the disturbing memories in all groups. All three groups combined resulted in strong positive relationships between the level of dental trait anxiety (DAS) and all of the memory characteristics (i.e., vividness, disturbance, sense of reliving, and level of intrusiveness and avoidance tendency; all *ps* < 0.001).

Table 4. Relation between dental trait anxiety (DAS) and memory characteristics in dental phobics, subthreshold dental phobics and normal controls

	Dental phobic		**Subthreshold dental phobic**		**Normal control**		**Overall**	
Memory characteristics	***r***	**n**	***r***	**n**	***r***	**n**	***r***	**N**
Emotional intensity								
Vividness	0.216*	39	0.145*	38	0.346***	49	0.557****	127
Disturbance	0.239*	39	0.082*	38	0.449****	49	0.582****	127
Sense of reliving	0.166*	39	0.263*	38	0.363***	49	0.582****	127
Intrusiveness and avoidance tendency								
IES total	0.360**	37	0.240*	33	0.727****	51	0.687****	121
IES intrusion	0.359***	37	0.235*	33	0.708***	51	0.649***	121
IES avoidance	0.320**	37	0.227*	33	0.691****	51	0.663****	121

***p > 0.05; ** p = 0.054; ***p < 0.05; **** p < 0.001**

Discussion

Limited research has been conducted on crucial and fear-evoking memories of individuals suffering from specific phobias. The present study examined not only the presence but also the content and some key characteristics of memories of events underlying dental

phobia, one of the most prevalent phobia subtypes in western societies (Oosterink et al., 2009).

The finding that both dental phobics and normal controls reported the presence of disturbing memories is in line with earlier findings (Liddell & Gosse, 1998; Locker et al., 1996). Further, the results supported our hypothesis that individuals with dental phobia would be significantly more likely to report such a memory than normal controls. Nearly all of the dental phobics reported a memory of an aversive or distressing event that they believed initiated or exacerbated their fear or phobia. Although in the present study, participants were explicitly asked about the memory 'that contributed most to their current anxiety', the proportion of dental phobics reporting a disturbing memory is comparable with reports of unpleasant memories of significant events in both individuals with other phobias, such as agoraphobia (100%; Day et al., 2004), and social phobia (96%; Hackmann et al., 2000). This suggests that having disturbing memories is a key feature of those suffering from pathological levels of anxiety and fear.

Another finding is that all participants recalled their most disturbing event as one that occurred in early adulthood, more than 20 years ago. Most of the memories were related to a disturbing dental event. This is in line with Pavlovian fear-conditioning theories (e.g., Davey, 1997), which predicts that irrational and pathological forms of dental anxiety are the result of previous exposure to aversive events within the dental setting (see also Moore et al., 1991; Oosterink et al., 2009). Conceivably, when individuals who have experienced a horrific dental incident are confronted with a stimulus situation comparable with the original incident, they feel overwhelmed by anxiety-eliciting memories. To this end, the present findings are supportive of the view that distressing events and their consequences, the disturbing memories of these experiences, play a critical role in the development and maintenance of dental anxiety.

Although it is known that memories of emotional (i.e., negative or positive) events vary highly between individuals (Haas & Canli, 2008) and are exacerbated in individuals with mood and anxiety disorders (e.g., PTSD; de Quervain et al., 2009; Haas & Canli, 2008), the present study is unique in its attempt to study differences in memory characteristics of individuals with dental phobia and normal controls. The results were supportive of our hypothesis in that the memories of the dental phobics were not only found to be significantly more vivid, disturbing, and displayed a significantly higher sense of reliving than the memories of the normal controls but also proved significantly more likely to show features typically seen in individuals suffering from PTSD (i.e., higher levels of intrusiveness and avoidance). Based on the memory identified during the memory interview, almost two-third (64.9%) of those suffering from dental phobia displayed these characteristics (i.e., IES ≥ 26). This is in sharp contrast with the normal control patients of which only a very small proportion (7.8%) showed such features. This similarity in trauma sequelae between dental anxiety and PTSD

corroborates the findings reported by previous studies (Oosterink et al., 2009; De Jongh et al., 2006, 2003, 2002).

The fact that the memory characteristics of individuals suffering from dental phobia resembled those with subthreshold dental phobia suggests that these groups should not be considered as separate entities but related conditions along a single continuum of severity of fear and anxious behavior (see also De Jongh et al., 2011). This is particularly relevant in the light of the concept of dimensionality introduced in the new version of the DSM (DSM-5; American Psychiatric Association, 2013), which allows more latitude regarding the assessment of the severity of a disorder with regard to defining a concrete threshold between 'normality' and a 'disorder'. It is conceivable that applying a strictly categorical model, as was carried out in previous editions of the DSM, might lead to situations that patients, who do not fulfill all criteria of a certain mental health condition, do not obtain the required treatment because of failure to meet a diagnostic threshold.

The third aim of the present study was to assess the relationship between a number of key phenomenological properties of patients' memories and severity of dental trait anxiety. Between both the patients with dental phobia and the normal controls, a significant positive association was found between greater level of intrusiveness and avoidance of the memory and severity of dental trait anxiety. Also patients' heightened sense of reliving was significantly related to level of dental trait anxiety. This is in line with a study on PTSD (Berntsen et al., 2003) showing that memory characteristics were associated with symptom severity. However, such a linear association in the domain of fears and phobias has not been established in earlier studies.

At the present time, recommended treatments of dental fear and phobias do not take into account the need to address disturbing memories but mainly involve a strict cognitive behavioral approach in which patients are exposed to their anxiety eliciting stimuli ('*in vivo* exposure') or carry out experiments that maximally violate expectancies about the frequency or intensity of possible aversive outcomes (Craske et al., 2014). It has been argued that such a procedure produces new memory representations that rival with previous learning and inhibit its effects (Brewin, 2006). The present findings may be considered as support for the feasibility of a different (i.e., 'trauma-focused') approach, namely one that is aimed to resolve patients' fear-related and disturbing memories, by directly changing the vividness and the disturbance of these memories, thereby inducing a long-lasting or permanent alleviation of the fear response (De Jongh et al., 2013; De Jongh et al., 2002; Doering et al., 2013). Yet, clearly, the most important advice is to prevent sensitization and accumulation of new disturbing memories by preventing the occurrence of negative events and the accompanying high levels of distress, during dental treatments.

This study has a number of limitations. Firstly, it is possible that at the time of the assessment, the dental phobic or subthreshold dental phobic individuals in the present sample

suffered from an episode of a mood or anxiety disorder, including depression and PTSD. These conditions can be comorbid in this patient group (e.g., Roy-Byrne et al., 1994) and affect the level of intrusion of aversive memories (Brewin, 2006), which might have confounded our results. In future studies on memory characteristics associated with specific phobia, the assessment of possible comorbidity needs to be taken into account. Secondly, a large number of patients with dental phobia and subthreshold dental phobia were unwilling to participate or canceled the appointment for the memory interview. It is likely that individuals with the highest levels of dental anxiety avoided participation in the present study. Therefore, current findings may be an underestimation of the differences between individuals with pathological levels of dental anxiety and low anxious individuals. Thirdly, because we sampled only patients from one dental fear clinic, our ability to generalize to other populations is limited. However, the fact that the present study comprised a relative small group of participants and that it was possible to obtain such strong results suggests that the effects are robust. Fourthly, the mean age in the normal control group was significantly higher than in the dental phobic and subthreshold dental phobic group. To investigate the possible effect of age, all data regarding memory characteristics were re-analyzed with age as a covariate; this did not affect the results or changed any of the outcomes of the study.

Apparently, having a memory of a distressing event that initiated or exacerbated dental anxiety is a common phenomenon not only in those suffering from dental phobia but also in those who are simply less apprehensive of dental treatment. Our findings indicate that individuals with dental phobia and subthreshold levels of dental phobia are likely to experience intrusive thoughts of earlier events associated with their fear. Such memories seem to share a number of key memory characteristics with trauma memories, like being vivid, disturbing, and uncontrollable. This suggests that specific phobias and fears are not simply a conditioned response to an initial neutral stimulus but one underpinned by the retrieval of stored memories following exposure to a negative or horrific event. Repeated triggering and re-experiencing of these memories are likely to play an important role in maintaining fears and specific phobias in that every reactivation of such disturbing memory further strengthens the aversive memory trace (De Quervain & Margraf, 2008). This means that activation of aversive memories not only plays an important role in the symptomatology of fears and phobias but also in the process contributing to the maintenance and aggravation of these symptoms.

References

Aartman, I. H. A., De Jongh, A., Makkes, P. C. & Hoogstraten, J. (2000). Dental anxiety reduction and dental attendance after treatment in a dental fear clinic: A follow-up study. Community Dentistry and Oral Epidemiology, 28: 435–442.

American Psychiatric Association. (2000). Diagnostic and statistical manual of mental disorders, DSM-IV-TR (4th edn). Washington, DC: American Psychiatric Association.

Arntz, A., de Groot, C. & Kindt, M. (2005). Emotional memory is perceptual. Journal of Behavior Therapy and Experimental Psychiatry, 36: 19–34.

Berntsen, D., Willert, M. & Rubin, D. C. (2003). Splintered memories or vivid landmarks? Qualities and organization of traumatic memories with and without PTSD. Applied Cognitive Psychology, 17: 675–693.

Brewin, C. R. (2006). Understanding cognitive behaviour therapy: A retrieval competition account. Behaviour Research and Therapy, 44: 765–784.

Clark, D. A. & Rhyno, S. (2005). Unwanted intrusive thoughts in nonclinical individuals: Implications for clinical disorders. In D. A. Clark (Ed.), Intrusive thoughts in clinical disorders: Theory, research, and treatment (pp. 1−29). New York: The Guilford Press.

Corah, N. L. (1969). Development of a dental anxiety scale. Journal of Dental Research, 48: 596.

Corah, N. L., Gale, E. N. & Illig, S. J. (1978). Assessment of a dental anxiety scale. The Journal of the American Dental Association, 97 :816–819.

Craske, M. G., Treanor, M., Conway, C. C. & Zbozinek, T. (2014). Maximizing exposure therapy: An inhibitory learning approach. Behaviour Research and Therapy, 58: 10–23.

Davey, G. C. L. (1997). A conditioning model of phobias. In G. C. L. Davey (Ed.), Phobias: A handbook of theory, research and treatment (pp. 301–322). Chichester, UK: Wiley.

Day, S. J., Holmes, E. A. & Hackmann, A. (2004). Occurrence of imagery and its link with early memories in agoraphobia. Memory, 12: 416–427.

De Jongh, A., Aartman, I. H. A. & Brand, N. (2003). Trauma-related symptomatology in anxious dental patients. Community Dentistry and Oral Epidemiology, 31: 52–58.

De Jongh, A., Ernst, R., Marques, L. & Hornsveld, H. (2013). The impact of eye movements and tones on disturbing memories of patients with PTSD and other mental disorders. Journal of Behavior Therapy and Experimental Psychiatry, 44: 447–483.

De Jongh, A., Fransen, J., Oosterink-Wubbe, F. M. D. & Aartman, I. H. A. (2006). Psychological trauma exposure and trauma symptoms among individuals with high and low levels of dental anxiety. European Journal of Oral Sciences, 114: 286–292.

De Jongh, A., Oosterink, F. M., Kieffer, J. M., Hoogstraten, J. & Aartman, I. H. A. (2011). The structure of common fears: Comparing three different models. The American Journal of Psychology, 124: 141–149.

De Jongh, A., van den Oord, H. J. M. & Ten Broeke, E. (2002). Efficacy of eye movement desensitization and reprocessing (EMDR) in the treatment of specific phobias: Four single-case studies on dental phobia. Journal of Clinical Psychology, 58: 1489–1503.

De Jongh, A., van der Burg, J., van Overmeir, M., Aartman, I. H. A. & van Zuuren, F. J. (2002). Trauma-related sequelae in individuals with a high level of dental anxiety: Does this interfere with treatment outcome? Behaviour Research and Therapy, 40: 1017–1029.

De Quervain, D. J., Aerni, A., Schelling, G. & Roozendaal, B. (2009). Glucocorticoids and the regulation of memory in health and disease. Frontiers in Neuroendocrinology, 30: 358–370.

De Quervain, D. J. & Margraf, J. (2008). Glucocorticoids for the treatment of post-traumatic stress disorder and phobias: A novel therapeutic approach. European Journal of Pharmacology, 583: 365–371.

Doering, S., Ohlmeier, M.-C., De Jongh, A., Hofmann, A. & Bisping, V. (2013). Eye movement desensitization and reprocessing (EMDR) for dental phobia – A pilot study. European Journal of Oral Sciences, 121: 584–593.

Ehlers, A., Hackmann, A., Steil, R., Clohessy, S., Wenniger, K. & Winter, H. (2002). The nature of intrusive memories after trauma: The warning signal hypothesis. Behaviour Research and Therapy, 40: 995–1002.

Engelhard, I. M., van den Hout, M. A., Arntz, A. & McNally, R. J. (2002). A longitudinal study of "intrusion-based reasoning" and PTSD after a train disaster. Behaviour Research and Therapy, 40: 1415–1424.

First, M. B. & Gibbon, M. (2004). The structured clinical interview for DSM-IV axis I disorders (structured clinical interview for DSM-IV-I) and the structured clinical interview for DSM-IV axis II disorders (SCID-II). In D. L. Segal & M. J. Hilsenroth (Eds.), Comprehensive handbook of psychological assessment, vol 2: Personality assessment (pp. 134–143). Hoboken, NJ: John Wiley.

Haas, B. W. & Canli, T. (2008). Emotional memory function, personality structure and psychopathology: A neural system approach to the identification of vulnerability markers. Brain Research Reviews 58: 71–84.

Hackmann, A., Clark, D. M. & McManus, F. (2000). Recurrent images and early memories in social phobia. Behaviour Research and Therapy, 38: 601–610.

Hackmann, A., Surawy, C. & Clark, D. M. (1998). Seeing yourself through others' eyes: A study of spontaneously occurring images in social phobia. Behavioural and Cognitive Psychotherapy, 26: 3–12.

Hagenaars, M. A. & Holmes, E. A. (2012). Mental imagery in psychopathology: Another step; Editorial for the special issue of journal of experimental psychopathology. Journal of Experimental Psychopathology, 3: 121–126.

Holmes, E. A., Grey, N. & Young, K. A. D. (2005). Intrusive images and "hotspots" of trauma memories in post-traumatic stress disorder: An exploratory investigation of emotions and cognitive themes. Journal of Behavior Therapy and Experimental Psychiatry, 36: 3–17.

Horowitz, M., Wilner, N. & Alvarez, W. (1979). Impact of event scale: A measure of subjective stress. Psychosomatic Medicine, 41: 209–218.

Kleber, R. J., Brom, D. & Defares, P. B. (1992). Coping with trauma. Theory, prevention and treatment. Lisse: Swets and Zeitlinger.

Liddell, A. & Gosse, V. (1998). Characteristics of early unpleasant dental experiences. Journal of Behavior Therapy and Experimental Psychiatry, 29: 227–237.

Locker, D., Shapiro, D. & Liddell, A. (1996). Negative dental experiences and their relationship to dental anxiety. Community Dental Health, 13: 86–92.

Michael, T., Ehlers, A., Halligan, S. L. & Clark, D. M. (2005). Unwanted memories of assault: What intrusion characteristics are associated with PTSD? Behaviour Research and Therapy, 43: 613–628.

Moore, R., Brødsgaard, I. & Birn, H. (1991). Manifestations, acquisition and diagnostic categories of dental fear in a self-referred population. Behaviour Research and Therapy, 29: 51–60.

Muse, K., McManus, F., Hackmann, A., Williams, M. & Williams, M. (2010). Intrusive imagery in severe health anxiety: Prevalence, nature and links with memories and maintenance cycles. Behaviour Research and Therapy, 48: 792–798.

Oosterink, F. M. D., De Jongh, A. & Aartman, I. H. A. (2009). Negative events and their potential risk of precipitating pathological forms of dental anxiety. Journal of Anxiety Disorders, 23: 451–457.

Oosterink, F. M. D., De Jongh, A. & Hoogstraten, J. (2009). Prevalence of dental fear and phobia relative to other fears and phobia subtypes. European Journal of Oral Sciences, 117: 135–143.

Oosterink, F. M. D., De Jongh, A., Hoogstraten, J. & Aartman, I. H. A. (2008). The level of exposure-dental experiences questionnaire (LOE-DEQ): A measure of severity of exposure to distressing dental events. European Journal of Oral Sciences, 116: 353–361.

Pratt, D., Cooper, M. J. & Hackmann, A. (2004). Imagery and its characteristics in people who are anxious about spiders. Behavioural and Cognitive Psychotherapy, 32: 165–176.

Reynolds, M. & Brewin, C. R. (1999). Intrusive memories in depression and posttraumatic stress disorder. Behaviour Research and Therapy, 37: 201–215.

Roy-Byrne, P. P., Milgrom, P., Khoon-Mei, T., Weinstein, P. & Katon, W. (1994). Psychopathology and psychiatric diagnosis in subjects with dental phobia. Journal of Anxiety Disorders, 8: 19–31.

Rubin, D. C., Feldman, M. E. & Beckham, J. C. (2004). Reliving, emotions, and fragmentation in the autobiographical memories of veterans diagnosed with PTSD. Applied Cognitive Psychology, 18: 17–35.

Veale, D., Murphy, P., Ellison, N., Kanakam, N. & Costa, A. (2013). Aversive memories of vomiting in people with a specific phobia of vomiting (emetophobia). Journal of Behavior Therapy and Experimental Psychiatry, 44: 14–20.

Whitaker, K. L., Brewin, C. R. & Watson, M. (2008). Intrusive cognitions and anxiety in cancer patients. Journal of Psychosomatic Research, 64: 509–517.

Looking back at last weeks' treatment, it wasn't so bad. But now, when I hear the drill, my heart rate rises and I am beginning to sweat. You are very kind, but I can't help wanting to leave the treatment room.

CHAPTER 5

Memory characteristics of an arousing event are associated with the level of anxiety during the event: a clinical study among individuals with severe dental anxiety

C.M.H.H. van Houtem, A.J. van Wijk, C. Kersten, A. de Jongh

Introduction

Extensive evidence indicates that adrenal stress hormones such as epinephrine and cortisol are critically involved in the formation of memories of emotionally arousing events (McGaugh & Roozendaal, 2002; Roozendaal, 2002; McGaugh, 2000). That is, the release of endogenous stress hormones not only give rise to an immediate response to an emotional event, but also aids future responses by enhancing the declarative memory of the same event (de Quervain et al., 2009; Cahill & Alkire, 2003; Roozendaal, 2002; McGaugh & Roozendaal, 2002; McGaugh, 2000; Cahill & McGaugh, 1998).

In this way exposure to distressing events create disturbing, emotionally charged memories that get re-activated by confrontations with objects of fear, while the related stress response induces an elevated heart rate (Leutgeb et al., 2011), emotional distress (Veale et al., 2013), and return of fear (Leutgeb et al., 2011; de Quervain et al., 2009; De Quervain & Margraf, 2008; Cuthbert et al., 2003). It has been argued that through this type of re-experiencing of past disturbing events and subsequent fear activations, memory traces get more and more ingrained (de Quervain et al., 2009; de Quervain & Margraf, 2008; Mathews & MacLeod, 2005; Pratt et al., 2004; Fehm & Margraf 2002; Clark, 1999).

Support for the notion that disproportionate levels of fear and anxiety are associated with presence of emotionally charged memories has been found in a study among dental phobic individuals (van Houtem et al., 2015). Their memories were found to be significantly more vivid, disturbing and displayed more features of intrusiveness than memories of less anxious controls. Moreover, it appeared that the disturbance of the memory of their most terrifying dental event and the severity of their current levels of dental trait anxiety were significantly associated (r = 0.58; van Houtem et al., 2015). Thus, activation of vivid emotional memories of past distressing events may not only play an important role in the symptomatology of fears and phobias, but also in the process contributing to the maintenance and aggravation of these conditions.

The notion that particularly emotionally significant experiences tend to be well remembered, is based upon memory consolidation and memory retrieval research (e.g., De Quervain & Margraf, 2008) and in laboratory settings (Talarico & Rubin, 2003; Heuer & Reisberg, 1990; Reisberg et al., 1988). However, to our knowledge it has hardly been explored in a clinical relevant situation (i.e., dental treatment) whether highly anxious individuals when confronted with potentially fear eliciting stimuli consolidate more vivid and disturbing memories of this event than their low anxious counterparts.

The purpose of the present study was to investigate how vividness and disturbance of a memory of a dental treatment changes over a two week period following this event. It was hypothesized that the memories of participants with a disproportional level of anxiety undergoing dental treatment would be significantly more vivid and disturbing than the

memories of the low anxious reference group, not only immediately after this event, but also at two-week follow up. In addition, it was hypothesized that the level of state anxiety during dental treatment and these memory characteristics would be positively associated.

Materials and methods

Measures

Presence of dental phobia
Presence of dental phobia was assessed using the Phobia Checklist, a screening tool with four questions based on the DSM-IV-TR criteria for specific phobia, developed for the assessment of dental phobia (Oosterink et al., 2009). This checklist contains four questions, and has previously been validated and proven to be a valid diagnostic tool for this purpose (sensitivity = 0.95, specificity = 0.99, and an overall hit rate of 97%).

Severity of dental trait anxiety
Dental trait anxiety was assessed using the Dental Anxiety Scale (DAS; Corah, 1969). This four item measuring scale is the questionnaire most widely used in studies on dental anxiety (Corah et al., 1978). Responses are scored from one to five, providing total scores ranging from four (not anxious at all) to 20 (extremely anxious). DAS scores of 13 or higher are considered indicative of high dental trait anxiety. Cronbach's alpha in the current study was 0.75 for anxious group and 0.80 for the reference group (overall $\alpha = 0.96$).

Level of state anxiety
Directly following treatment (T1) and at two-week follow-up (T2) participants were asked to indicate the extent to which they felt anxious during dental treatment using an 11-point numeric rating scale (NRS; 0 = minimum level of anxiety, 10 = maximum level of anxiety).

Memory characteristics
Immediately following a conventional dental treatment (T1) and at two weeks follow-up (T2) disturbance and vividness of the memory about the dental treatment was indexed using an 11-point NRS (0 = not at all disturbing/vivid and 10 = maximum level of disturbance/vividness).

Participants

The study included two groups of participants: 1) those with severe levels of dental trait anxiety (i.e., participants with a DAS-score ≥ 13; further referred to as 'the anxious group')

and 2) those with low levels of dental trait anxiety (i.e., DAS <13; further referred to as 'the reference group'). Participants of the anxious group were attending a special dental fear clinic in Amsterdam, the Netherlands. They were referred to the clinic because they were extremely difficult or impossible to treat by a dentist in a general dental practice due to disproportionate anxiety levels, or showed anxiety-related avoidance of the dental treatment. The reference group consisted of participants who attended a regular dental practice in three different cities in the Netherlands. Participants were included in the study if they were 18 years or older, had sufficient control of the Dutch language and gave written consent to participate.

Study design and procedure

The study was conducted between March 2010 and June 2012 and was based on a prospective design with two assessment points (T1-T2). At baseline (T0), all participants of both groups were invited by telephone to take part in a study concerning autobiographical memories underlying dental anxiety. Those who were willing to participate were checked whether or not they fulfilled the inclusion criteria. The participants received a letter at home containing additional information, a consent form, and a request to fill out several measures on severity of dental trait anxiety or dental phobia. Prior to the current study the participants were included in a study that investigated the presence, content and characteristics of memories events underlying dental anxiety (for a comprehensive description of the data collection, sample and study design see van Houtem et al., 2015). For the purpose of the current study participants were asked to complete a self-report questionnaire that assessed the disturbance and vividness of their memory of an invasive (i.e., drilling and making a filling, carrying out a root canal treatment or an extraction) dental treatment as well as their level of state anxiety during treatment immediately following this treatment (T1). Two weeks later participants of both groups were contacted by telephone and were asked to bring up the memory of the treatment that was performed two weeks before. Then their memory characteristics were re-assessed (T2). Ethical approval for the study was granted by the local Ethical Committee (METc VU, protocol number 2007/262).

Statistical analyses

Descriptive statistics were used to characterize the sample. Chi-square tests (categorical data) or student's t-tests (continuous data) were used to examine group differences at T1 and T2. Two-way MANOVA's on the set of dependent variables (state anxiety, disturbance and vividness) were used to investigate the possible interaction between group and gender at T1 and T2. In order to test group differences in the changes over time between T1 and T2 on the set of dependent variables, a two-way repeated measures MANOVA (one-within [time] and one-between subjects factor [group]) was used. A MANCOVA was performed on

the difference score between T1 and T2, using the score at T1 as a covariate, thereby correcting the change score for differences at baseline. The Pearson correlation coefficient was used as a measure of linear association. Power calculation (G*Power 3.0; Faul, Erdfelder, Lang & Buchner, 2007) based on an independent samples T-test and based on a large effect size (0.8), alpha = 0.05, power = 0.80 and two-tailed testing, resulted in a minimum required total sample size of *n* = 52. For all statistical analyses, a p-value <0.05 was considered statistically significant.

Results

General differences between both groups

The final sample consisted of 114 participants (i.e., 47 anxious and 67 reference individuals) with a mean age of 44.6 years (SD = 12.4) and resp. 51.8 years (SD = 15.1). Table 1 shows the demographic characteristics in male and female participants of both groups at baseline (T0). There was no significant difference in terms of gender (*p* = 0.39) and a marginal significant difference in country of birth *(p* = 0.06) between the anxious individuals and the reference group of low anxious individuals.

Of the participants in the anxious group 60.1% (n = 25) fulfilled all screening criteria for dental phobia, whereas none of the reference group fulfilled these criteria (0.0%; $\chi^2(1)$

Table 1. Demographics and mean level of dental trait anxiety of the anxious and low-anxious reference participants at baseline (T=0)

	Anxious (n=47)			**Reference (n=67)**				
	Percentage		**n**	**Percentage**		**n**	***P***	**χ2**
Gender								
Male	42.5		20	50.8		34	0.39	0.74
Female	57.5		27	49.3		33		
Country of birth								
Dutch	83.0		39	94.0		63	0.06	3.58
Other	17.0		8	6.0		4		
	Mean	**±SD**	**n**	**Mean**	**±SD**	**n**	***p***	**T**
Age in years								
Total	44.6	12,4	46	51.8	15,1	67	<0.01	-2.76
Male	42.1	9,4	19	53.5	14,7	34	<0.01	-3.46
Female	46.3	14,1	27	49.9	15,6	33	0.35	-0.93
Dental trait anxiety (4-20)								
Total	17.6	2.3	47	7.2	1.9	67	<0.01	25.8
Male	17.2	2.6	20	7.2	2.0	34	<0.01	14.9
Female	17.9	2.0	27	7.3	1.7	33	<0.01	21.6

= 53.16, p = 0.01). Participants of the anxious group showed significantly higher levels of dental trait anxiety (17.55 ± 2.26), than individuals of the reference group (7.22 ± 1.87; t (86.58) = 25.75, p < 0.001).

State anxiety, vividness and disturbance of the memory of dental treatment at T1 and T2

The anxious and reference group were compared immediately after treatment (T1) on state anxiety, disturbance and vividness using a two-way (group by gender) MANOVA. Mean scores are presented in Table 2. A significant multivariate effect for group was found, F (3, 106) = 26.47, p < 0.001, and no significant effect for gender, F (3, 106) = 1.31, p = 0.28, nor an interaction between group and gender, F (3, 106) = 1.30, p = 0.28. The significant group effect resulted from a higher mean score of the anxious group on state anxiety, F (1, 108) = 51.53, p < 0.001, on disturbance, F (1, 108) = 55.07, p < 0.001, and on vividness, F (1, 108) = 39.20, p < 0.001, than the reference group.

Another two-way MANOVA was performed (T2) to compare both groups on disturbance and vividness at two weeks follow up (see Table 2). The results showed a significant multivariate main effect for group, F (2, 92) = 18.80, p < 0.001, no significant effect for gender, F (2, 92) = 0.71, p = 0.493, nor an interaction between group and gender, F (2, 92) = 1.35, p = 0.266. The significant group effect resulted from a higher mean score of the anxious group on disturbance, F (1, 93) = 27.07, p < 0.001, and on vividness, F (1, 93) = 29.25, p < 0.001, than the reference group.

A two-way (time by group) repeated measures MANOVA was performed to compare the anxious and reference group in changes in disturbance and vividness over time. The results showed a significant multivariate main effect for time, F (2, 91) = 14.94, p < 0.001, but no significant interaction, F (2, 91) = 0.25, p = 0.781. The main effect for time resulted

Table 2. Mean scores* of disturbance and vividness immediately after treatment (T1) and after two weeks (T2) in the anxious and reference group

	Measure	T1			T2		
		Mean	SD	N	Mean	SD	N
Anxious	State anxiety	4.83	2.98	46	-	-	-
	Disturbance	3.96	3.04	46	3.85	2.65	41
	Vividness	7.13	3.22	46	5.22	3.02	41
Reference	State anxiety	1.35	2.04	66	-	-	-
	Disturbance	.64	1.62	66	1.27	2.21	56
	Vividness	3.09	3.33	66	2.00	2.81	56
Total	State anxiety	2.78	3.00	112	-	-	-
	Disturbance	2.00	1.62	112	2.36	2.72	97
	Vividness	4.75	3.83	112	3.36	3.30	97

* Mean scores and standard deviations are based on all available data at T1 and T2

from a significant decrease in disturbance, F (1, 92) = 6.03, *p* = 0.016, and vividness, F (1, 92) = 14.62, *p* < 0.001. In the anxious group a non-significant increase for disturbance (t (38) = 1.33, *p* = 0.19) was found and a significant decrease for vividness (t (38) = -2.55, *p* = 0.015) over time. In the reference group a significant increase in disturbance (t (55) = 2.46, *p* = 0.17) and a significant decrease in vividness (t (54) = -2.67, *p* = 0.006) was found.

However, since the differences at T1 between the anxious and the reference group on the variables disturbance and vividness may have affected the change over time, the two groups were compared on the difference score between T1 and T2 on the variables disturbance and vividness, using the scores at T1 as covariates in a MANCOVA. The results from this analysis showed that disturbance was a significant covariate for the disturbance, F (1, 90) = 11.51, p <0.001, and vividness, F (1, 90) = 5.28, p = 0.024 change score, and vividness was a significant covariate for the vividness change score, F (1, 90) = 76.91, p < 0.001, but not for disturbance, F (1, 90) = 1.33, p = 0.25. As a result, mean change scores on both variables were adjusted for differences on the score at T1. In this adjusted analysis, a significant multivariate group effect was found, F (2, 89) = 3.93, p = 0.023, indicating that both groups differ in the changes in mean scores over time. Inspection of the adjusted mean scores reveals that the anxious group (mean difference = -0.46, 95% CI [-1.40 – 0.47]) reported a significantly smaller reduction of vividness than the reference group (mean difference = -1.98, 95% CI [-2.7 - -1.22]), and a larger increase in disturbance (mean difference = 1.17, 95% CI [0.50 – 1.83]) than the reference group (mean difference = 0.01 95% CI [-0.53 – 0.55]). Changes on the outcome variables between T1 and T2 for each group are presented in Figure 1.

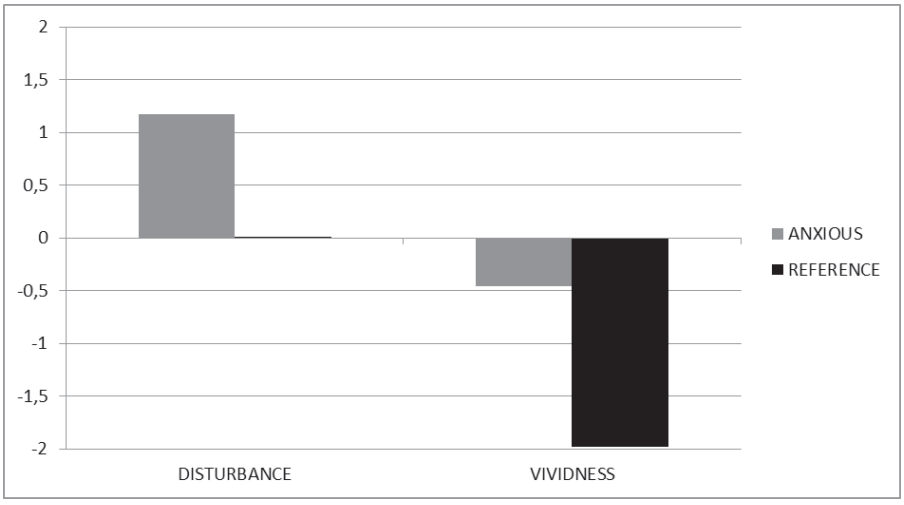

Figure 1. Adjusted mean difference scores between T1 and T2 for the variables disturbance and vividness for the anxious and the low-anxious reference group*
* The difference in disturbance between T1 n T2 in the control group is not visible, since the difference was only 0.01 on an 11 point NRS.

Relation between state anxiety and memory characteristics of the disturbing memory

Among the anxious participants the correlations between state anxiety during dental treatment, and either vividness or disturbance of the memory two weeks following treatment did not reach significance ($r = 0.19$, $p = 0.24$ and $r = 0.20$, $p = 0.24$, respectively). Among the reference group positive significant correlations were found between state anxiety during treatment and both memory characteristics two weeks later ($r = 0.60$, $p < 0.001$ and $r = 0.31$, $p = 0.021$, respectively). To avoid a lack of variance as a result of both floor effects and ceiling effects both groups were combined. A normality test showed that the data were well modeled by a normal distribution. Table 3 displays the correlation coefficients at both time points among the variables state anxiety during dental treatment, vividness and disturbance for both groups combined (total n at T1 = 112 and total n at T2 = 93). As can be seen, level of state anxiety during dental treatment significantly predicted the extent to which participant' memories were experienced as vivid ($r = 0.46$, $p < 0.001$) and disturbing ($r = 0.55$, $p < 0.001$) two weeks following treatment.

Table 3. Association between state anxiety during treatment and the memory characteristics 'vividness' and 'disturbance' at both time points for the total group (anxious and reference patients collapsed).

		state anxiety (T1)	disturbance (T1)	vividness (T1)
T1	state anxiety	1.00		
	disturbance	0.768**	1.00	
	vividness	0.499**	0.477**	1.00
T2	disturbance	0.551**	1.00	
	vividness	0.457**	0.577**	1.00

**$p < 0.001$

Discussion

The results of the present study indicate that individuals with severe levels of anxiety about dental treatment reported their memory of a dental treatment to be significantly more vivid and more disturbing than participants' memories with no or almost no anxiety. This was not only found immediately following treatment, but also at two weeks follow-up.

Both the anxious and the reference participants displayed changes in vividness of their memories in that these became significantly less vivid over a two-week period. This decline can probably best be explained by a logarithmic degrading of memories over time (Wixted & Carpenter, 2007; Talarico & Rubin, 2003). Interestingly, the disturbance of the memory showed a different pattern. While the disturbance of the memories in the reference group remained stable, the disturbance of the memories of the anxious individuals increased. Most

likely, the results of our study can best be explained in the light of findings of studies examining emotional arousal and memory performance in individuals with PTSD (e.g., Wilker et al., 2014; Paunovic et al., 2002), showing that subjects with PTSD display enhanced memory for emotionally arousing information compared with healthy controls (Wilker et al., 2014; Golier et al., 2003). Precisely this fact may explain the increased memory disturbance of anxious individuals in our study. In individuals with disproportionate levels of anxiety, exposure to a phobic stimulus almost invariably provokes retrieval of the fear memory, thereby triggering an adrenal stress response (De Quervain et al., 2011; Alpers et al., 2003) which would, in turn, lead to enhanced storage of emotional memories (McIntyre & Roozendaal, 2007).

Our most striking finding was that individuals' state anxiety level during dental treatment was significantly linearly associated with the extent to which the memories of this event were reported as emotionally charged. The best explanation for this phenomenon is that the more physiological arousal was elicited by the event, the more the memory was experienced as emotionally disturbing and vivid. This is in line with a wide array of laboratory (Anderson et al., 2006; Ochsner, 2000) and experimental studies showing a positive linear relationship between the degree of stress experienced during a fearful event, and the strength of the fear-conditioned memory that was formed in relation to the level of adrenal stress hormones (Laxmi et al., 2003; Cordero et al., 1998). To our knowledge, such a relationship for the effects of physiological and emotional arousal (in our study operationalized as state anxiety) in the formation of fear memories has not previously been demonstrated in a relevant clinical setting such as dentistry.

This study has some limitations. First of all, we were not able to match individuals of the anxious and reference group in terms of gender and age, since more anxious participants than we expected appeared to be unwilling to fill out the questionnaire immediately after the dental treatment. Next, the level of physiological or emotional arousal in this study was only assessed by a self-report measure indexing state anxiety (i.e., an 11-point NRS). Although self-reported state anxiety has been found to correlate significantly with heart rate (Kantor et al., 2001), in future studies it would be important to replicate the current findings using physiological and biological outcome variables in order to more specifically investigate the factors mediating the activation of the human stress response system. More general, and in relation to future research, translational studies in relevant clinical settings that examine possible individual differences in responsiveness to acute stress and emotional memory, are greatly needed. A possible direction would be to examine whether specific genetic variations (e.g. of the ADRA2B gene; Rasch et al., 2009; de Quervain et al., 2007) involved with noradrenergic neurotransmission are associated with elevated levels of dental trait anxiety and enhanced emotional memory of emotionally arousing events (Li et al., 2015).

In conclusion, the present results suggest that individuals' state anxiety level during a dental treatment is predictive of the extent to which the memory of such an event becomes

emotionally charged. Furthermore, the results provide evidence for a linear relationship between emotional arousal on the formation of fear memories entailing possible clues for the role of emotional responses induced by anxiety eliciting and potentially dangerous situations which enables us to remember the significance of such events. Our results may also have important clinical implications. Dental practitioners or other health care professionals should be cautionary that anxiety levels during their procedures may increase far above the normal or average range, thereby cementing new aversive memory traces (De Quervain et al., 2009), a process which may explain why existing anxiety levels are maintained or even further increase.

References

Alpers, G.W., Abelson, J.L., Wilhelm, F.H. & Roth, W.T. (2003). Salivary cortisol response during exposure treatment in driving phobics. Psychosomatic Medicine, 65: 679-87.

Anderson, A.K., Wais, P.E. & Gabrieli, J.D (2006). Emotion enhances remembrance of neutral past. Proceedings National Academy of Science U. S. A., 103: 1599-604.

Cahill, L. & McGaugh, J.L., (1998). Mechanisms of emotional arousal and lasting declarative memory. Trends in Neuroscience. 21: 294–299.

Cahill, L. & Alkire, M. T. (2003). Epinephrine enhancement of human memory consolidation: Interaction with arousal at encoding. Neurobiology of Learning and Memory. 79: 194-198.

Clark, D.M. (1999). Anxiety disorders: why they persist and how to treat them. Behaviour Research and Therapy, 37, Suppl 1: S5-27.

Corah, N. L. (1969). Development of a dental anxiety scale. Journal of Dental Research, 48: 596.

Corah, N.L., Gale, E.N. & Illig, S.J. (1978). Assessment of a dental anxiety scale. The Journal of the American Dental Association, 97: 816-819.

Cordero, M.I., Merino, J.J. & Sandi, C. (1998). Correlational relationship between shock intensity and corticosterone secretion on the establishment and subsequent expression of contextual fear conditioning. Behaviour Neuroscience, 112: 885-91.

Cuthbert, B. N., Lang, P. J., Strauss, C., Drobes, D., Patrick, C. J. & Bradley, M. M. (2003), The psychophysiology of anxiety disorder: Fear memory imagery. Psychophysiology, 40: 407–422.

De Quervain, D.J.F., Kolassa, I.T., Ertl, V., Onyut, P.L.,Neuner, F. Elbert, T. & Papassotiropoulos, A. (2007). A deletion variant of the α2b-adrenoceptor is related to emotional memory in Europeans and Africans. Nature Neuroscience, 10: 1137 – 1139.

De Quervain, D.J. & Margraf J. (2008). Glucocorticoids for the treatment of post-traumatic stress disorder and phobias: A novel therapeutic approach. European Journal of Pharmacology, 583: 365–371.

De Quervain, D.J., Aerni, A., Schelling, G. & Roozendaal, B. (2009). Glucocorticoids and the regulation of memory in health and disease. Frontiers in Neuroendocrinology, 30: 358-370.

De Quervain, D.J.F., Bentz, D., Michael, T., Bolt, O.C., Wiederhold, B.K., Margraf, J. & Wilhelm, F.H. (2011). Glucocorticoids enhance extinction-based psychotherapy, 108: 6621–6625.

Faul, F., Erdfelder, E., Lang, A.-G. & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behavior Research Methods,39: 175-191.

Fehm, L. & Margraf, J. (2002). Thought suppression: specificity in agoraphobia versus broad impairment in social phobia? Behaviour Research and Therapy, 40: 57-66.

Golier, J.A., Yehuda, R., Lupien, S.J. & Harvey, P.D. (2003). Memory for trauma-related information in Holocaust survivors with PTSD. Psychiatry Research, 121: 133-43.

Heuer, F. & Reisberg, D. (1990). Vivid memories of emotional events: The accuracy of remembered minutiae. Memory & Cognition, 18: 496-506.

Kantor, L., Endler, N.S., Heslegrave, R.J. & Kocovski, N.L (2001). Validating self-report measures of state and trait anxiety against a physiological measure. Current Psychology, 20: 207-215.

Laxmi, T.R., Stork, O. & Pape, H.C. (2003). Generalization of conditioned fear and its behavioural expression in mice. Behavioural Brain Research, 145: 89–98.

Leutgeb, V., Schafer, A. & Schienle, A. (2011). Late cortical positivity and cardiac responsitivity in female dental phobics when exposed to phobia-relevant pictures. International Journal of Psychophysiology. 79: 410–416.

Li, S., Weerda, R., Milde, C., Wolf, O.T. & Thiel, C.M. (2015). ADRA2B genotype differentially modulates stress-induced neural activity in the amygdala and hippocampus during emotional memory retrieval. Psychopharmacology, 232: 755-764.

Mathews, A. & MacLeod, C. (2005). Cognitive vulnerability to emotional disorders. Annual Review of Clinical Psychology, 1: 167-195.

McGaugh, J.L. (2000). Memory: a century of consolidation. Science, 287: 248-51.

McGaugh, J. L. & Roozendaal, B. (2002). Role of adrenal stress hormones in forming lasting memories in the brain. Current Opinion in Neurobiology, 12: 205–210.

McIntyre, C.K. & Roozendaal, B. (2007). Neural Plasticity and Memory: From Genes to Brain Imaging. Chapter 13: Adrenal Stress Hormones and Enhanced Memory for Emotionally Arousing Experiences. Bermúdez-Rattoni F., editor, Boca Raton (FL): CRC Press.

Oosterink, F.M., De Jongh, A. & Hoogstraten, J. (2009). Prevalence of dental fear and phobia relative to other fear and phobia subtypes. European Journal of Oral Science, 117: 135-143.

Ochsner, K. N. (2000). Are affective events richly recollected or simply familiar? The experience and process of recognizing feelings past. Journal of Experimental Psychology: General, 129: 242-261.

Pratt, D., Cooper, M.J. & Hackmann, A. (2004). Imagery and its characteristics in people who are anxious about spiders. Behavioural and Cognitive Psychotherapy, 32: 165–176.

Paunovic, N., Lundh, L.G. & Ost, L.G (2002). Attentional and memory bias for emotional information in crime victims with acute posttraumatic stress disorder (PTSD). Journal of Anxiety Disorders, 16: 675–692.

Rasch, B. Spalek, K., Buholzer, S., Luechinger, R., Boesiger, P., Papassotiropoulos, A. & de Quervain, D.J. (2009). A genetic variation of the noradrenergic system is related to differential amygdala activation during encoding of emotional memories. Proceedings of the National Academy of Sciences of the United States of America, 106: 19191-19196.

Reisberg, D., Heuer, F., Mclean, J. & O'Shaughnessy, M. (1988). The quantity, not the quality, of affect predicts memory vividness. Bulletin of the Psychonomic Society, 26: 100-103.

Roozendaal, B. (2002). Stress and Memory: Opposing Effects of Glucocorticoids on Memory Consolidation and Memory Retrieval. Neurobiology of Learning and Memory, 78: 578–595.

Talarico, J.M. & Rubin, D.C. (2003). Confidence, not consistency, characterizes flashbulb memories. Psychological Science, 14: 455-461.

van Houtem, C. M. H. H., van Wijk, A. J. & De Jongh, A. (2015). Presence, content, and characteristics of memories of individuals with dental phobia. Applied Cognitive Psychology, 29: 515-523.

Veale, D., Murphy, P., Ellison, N., Kanakam, N. & Costa, A. (2013). Autobiographical memories of vomiting in people with a specific phobia of vomiting (emetophobia). Journal of Behavior Therapy and Experimental Psychiatry, 44: 14-20.

Wixted, J.T. & Carpenter, S.K. (2007). The Wickelgren power law and the Ebbinghaus savings function. Psychological Science, 18: 133-134.

Wilker, S., Elbert, T. & Kolassa, I. T. (2014). The downside of strong emotional memories: How human memory-related genes influence the risk for posttraumatic stress disorder – A selective review. Neurobiology of Learning and Memory, 112: 75-86.

As long as I can remember I feel dizzy when I receive an injection. Sometimes I actually faint and that delays and impedes the treatment. It is not that I'm afraid of injections, but it will be clear that I don't like fainting. That is why I'm feeling nervous entering the treatment room.

CHAPTER 6

Is dental phobia a blood-injection-injury phobia?

C.M.H.H. van Houtem, I.H.A. Aartman, D. I. Boomsma,
L. Ligthart, C.M. Visscher & A. de Jongh

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Introduction

Specific phobia is an anxiety disorder that represents unreasonable or irrational fear of a specific object or situation (Craske et al., 1996). One of the specific phobia subtypes retained in the Diagnostic and Statistical Manual of Mental Disorders (DSM–IV–TR) is Blood-Injection-Injury (B-I-I) phobia, a phobic condition involving an extraordinary fear of blood, injuries, needles, and invasive medical procedures (APA, 2000). B-I-I phobia usually starts in childhood (Bienvenu & Eaton, 1998), is often familial (Page, 1994; Kleinknecht & Lenz, 1989; Marks, 1988; Kozak & Montgomery, 1981), shows prevalence rates of about 3% (Bienvenu & Eaton, 1998; Fredrikson et al., 1996; Neale et al., 1994), and is more prevalent in women than in men (Bienvenu & Eaton; Agras, Sylvester, Oliveau, 1969). There are indications that of all specific phobia subtypes B-I-I phobia is most strongly associated with disability (Burstein et al., 2012).

According to the text of the DSM-IV-TR (p. 446; APA, 2000), B-I-I phobia is characterized by a strong vasovagal response, also referred to in the literature as a biphasic response pattern. This response is supposed to consist of an initial acceleration in heart rate and increase in blood pressure, followed by a heart rate deceleration and blood pressure drop leading to an increased likelihood of vasovagal fainting (APA, 2000; Page, 1994; Öst et al., 1984). It is assumed that about 75% of patients afflicted with B-I-I phobia have a history of fainting in phobia-relevant situations (APA, 2000).

Dental phobia is a disproportional fear of (invasive) dental procedures, and is currently classified as a specific phobia of the B-I-I subtype within DSM-IV-TR. Regarding the convergent and discriminant validity of this categorization, there are only two factor analytic studies that specifically attempted to determine whether dental fear corresponds to the cluster of fears within the B-I-I subtype of specific phobia. Both studies found support for a classification of fears with a B-I-I or "mutilation" factor comprising fears of injections, injuries, and dental treatment (De Jongh et al., 2011; Fredrikson et al., 1996). Conversely, a study assessing the relationship between dental anxiety, and either B-I-I anxiety or B-I-I avoidance among dental patients found only weak nonsignificant correlations between these constructs (r = 0.16 and –0.02, respectively; De Jongh et al., 1998). Further, a community survey showed that among dentally anxious individuals, only 16% could also be classified as blood-injury fearful (Locker et al., 1997). Vice versa, a study among blood and injection phobics showed that less than 20% of them also had a strong fear of the dental situation (Öst, 1992). The small level of co-occurrence of dental fear in general and typical B-I-I fears seems to challenge the contention that dental fear is a typical B-I-I fear.

The question whether dental phobia is a B-I-I phobia also pertains to onset, phenomenology, and treatment planning. Whereas the origin of dental phobia could easily be explained as the result of associative learning (De Jongh et al., 1998), the origins of fear of blood and

injury have been claimed to largely lie in genetic factors (Page & Martin, 1998; Neale et al., 1994). Even more striking are the differences in physiological response pattern between dental phobia and B-I-I phobia. Whereas B-I-I phobia is associated with a biphasic response pattern, the cardiac reaction in dental phobics during exposure to phobic stimuli is typically associated with an acceleration of heart rate, which is not followed by a drop in heart rate (Leutgeb et al., 2011; Schmid-Leuz et al., 2007; Elsesser et al., 2006; Johnson et al., 2003; Lundgren et al., 2001), and fainting (De Jongh et al., 1998; Leutgeb et al., 2011). Another area in which dental phobia differs from B-I-I phobia is the treatment of both conditions. While in vivo exposure to anxiety provoking stimuli is generally considered to be the most appropriate treatment for specific phobia in general (De Jongh et al., 2005), for B-I-I phobia, when the patient presents with a vasovagal fainting response, the preferred additional treatment is "applied tension" (i.e. artificially increasing the blood pressure by tensing the muscles; Ayala et al., 2009; Öst et al., 1991).

Taken together, the findings of studies that investigated the dynamic of dental phobia cast doubt on the empirical basis of the current classification of dental phobia as a "pure" B-I-I phobia within DSM-IV-TR. Yet, in the light of the development of DSM-5, the authors of a recent paper evaluating the current diagnostic criteria for specific phobia, concluded that "*dental phobia shares more similarities than differences with B-I-I phobia* (LeBeau et al., 2010)." To further elucidate this issue the purpose of the present study was to investigate the conceptual validity of the DSM classification of dental phobia within the B-I-I phobia subtype of specific phobia. Therefore, the co-occurrence of dental phobia, fear of dental objects and situations (including B-I-I-related stimuli), and a history of vasovagal fainting during dental treatment was investigated. More specifically, based on the current classification of dental phobia as a B-I-I phobia subtype within DSM we expected to find that dental phobics would rate B-I-I-related stimuli equally anxiety provoking as typically dental-related stimuli. Secondly, it was hypothesized that there would be relatively more individuals with a fainting history among dental phobics than among non-dental phobics.

A related issue concerns the contribution of dizziness and fainting to the tendency to avoid situations where fainting might occur (i.e. the dental treatment). For B-I-I phobia it has been claimed that fainting in response to B-I-I stimuli can aggravate avoidance of medical care (Kleinknecht & Lenz, 1989), which could exacerbate medical conditions and may lead to health threatening situations (APA, 2000; Bienvenue & Eaton, 1998; Page, 1994). If dental phobic individuals indeed display a similar distinctive autonomic reaction and a selective propensity to faint as seen in "pure" B-I-I phobics, it is conceivable that this response pattern would evoke a fear of fainting and preclude individuals securing appropriate care with detrimental effects on oral health. Remarkably, however, besides the text of the DSM-IV that states that "*Specific Phobias of the Blood-Injection-Injury Type, may have detrimental effects on dental and physical health, because the individual may avoid obtaining necessary*

medical care" (p. 446; APA, 2000) and suggestions in this direction (Ayala et al., 2009; Marks, 1998; Hamilton, 1995; Page, 1994) we are not aware of any study supporting such a claim in relation to dental phobia. Therefore, the third aim was to test the hypothesis that fainting would be significantly associated with avoidance of dental care.

Methods

Research participants

This study is part of an ongoing study on lifestyle and personality in twin families registered with the Netherlands Twin Register (NTR; Boomsma et al., 2006). The data are derived from the 9th wave of survey collection in adult participants that was carried out in 2011 and 2012. After obtaining approval from the Medical Ethics Committee of the VU University Medical Center Amsterdam, NTR participants aged 18 years and older were invited to complete the survey (*N* = 27,892). At the time of analysis, 11,225 subjects had responded (response rate 40.2%). Twelve participants were excluded because of missing data on family structure (*n* = 6), age (*n* = 3) or because they were younger than 18 years (*n*= 3). The remaining subjects (*n* = 11,213 of 5,098 families) had a mean age (±SD) of 44.26 (±15.42) years (age range 18–100 years) with 61.2% being female. Participants were mostly born in the Netherlands (97.4%).

Procedure

Participants were sent a written invitation including a link to the web page where they could log on to a web-based survey with a unique, personal login name and password. Subjects who had not yet accessed the web-based survey within three months after the first invitation received a written reminder. For participants without internet access, a hard copy version of the survey was available on request. In this study, only data of the web-based survey were used in the analyses (*n* = 11,213).

Measures

Sociodemographics

The questionnaire included questions about sex and age. Information on country of birth was available for 6,530 individuals and level of education was available for 8,082 individuals based on previous questionnaires (Willemsen et al., 2013).

Presence of Dental Phobia

Presence of dental phobia was assessed using the Phobia Checklist, a screening tool with four questions based on the DSM-IV-TR criteria for specific phobia (APA, 2000), developed

for the assessment of dental phobia. This instrument has previously been validated and proven to be a valid diagnostic tool for this purpose (sensitivity = 0.95, specificity = 0.99, and an overall hit rate of 97%; Oosterink et al., 2009). The Phobia Checklist contains the following four questions: (i) When I see or undergo dental treatment I feel unreasonable or excessive (= very strong) anxiety; (ii) I try to avoid dental treatment, or else I undergo treatment only with great anxiety; (iii) I see that I am far more anxious of dental treatment than is justified; and (iv) My fear or avoidance of dental treatment is significantly interfering with or restricting my life. Dental phobia was considered present when all four questions were answered in the affirmative.

Severity of Dental Fear

Severity of dental fear was assessed using the Dental Anxiety Scale (Corah, 1969). Responses are scored from 1 to 5, providing total scores ranging from 4 (not anxious at all) to 20 (extremely anxious). DAS scores of 13 or higher are considered indicative of the presence of a high level of dental fear (Corah et al., 1978). Cronbach's alpha of the DAS in the current study was 0.90.

History of Fainting During Dental Treatment

History of dizziness or fainting during dental treatment was assessed with the dichotomous question "*Did you ever feel dizzy or did you ever faint during a dental treatment?*"

Anxiety Provoking Stimuli

The fear provoking nature of 28 stimuli was assessed using the question: "Below you will find examples that you may have experienced at the dentist, oral hygienist, or oral surgeon. Please indicate for each example whether this evokes a fear response?" The stimuli were derived from a questionnaire with 67 potentially anxiety-provoking objects and situations related to the dental setting (Oosterink et al., 2008). In the current study, only the 25 most prevalent anxiety-provoking stimuli were used as items for the questionnaire, which was supplemented with three additional stimuli (i.e. gagging, a sense of vomiting, and fainting). The questionnaire contained the following B-I-I-related stimuli: having surgery, being injured, receiving an injection, and seeing blood. Each of the items were scored on a four point scale, from 1 (not anxiety provoking at all) to 4 (extremely anxiety provoking).

Avoidance of Dental Care

An established way to index regular dental attendance is to assess the proportion of people who visit the dentist at least once a year (Mulder, 2010). Accordingly, those who reported visiting a dentist less than once a year during a 5-year period were classified as having a

tendency to avoid dental care. This was scored using two distinct categories (i.e. regular attendance or avoidance of dental care).

Statistical analyses

Descriptive statistics were performed in IBM SPSS Statistics (Version 20). Regression analyses (continuous measures) and logistic regression (categorical measures) were carried out in STATA 12.1 (StataCorp, College Station, Texas, USA) to test whether dental phobia, fainting, and avoidance were related to a selection of variables. STATA's "robust cluster" option was used to account for the nonindependence of family members. The strength of the associations between avoidance of dental care on the one hand, and a selection of variables on the other, was estimated by the odds ratio (OR) and 95% confidence intervals. To cross-validate findings based on the relatively small number of strict dental phobics, analyses were partially repeated using a distinction between high and low levels of dental fear based on the DAS. For all statistical analyses, a *P*-value < 0.05 was considered statistically significant.

Results

Sample characteristics

Sociodemographic characteristics are reported in Table 1 for participants with (*n* = 48, 0.4%) and without a dental phobia, for participants with a history of dizziness or fainting during dental treatment (*n* = 472, 4.3%) or not and for participants who avoided dental care (*n* = 2,010, 18.1%) or not. Comparisons between these groups revealed that a gender difference was present for fainting history during dental treatment and for avoidance of dental care.

Anxiety provoking stimuli as indicated by individuals with and without dental phobia

Table 2 shows the mean scores of anxiety provoking stimuli as rated by those with and without dental phobia, and the proportion of them rating a specific stimulus as extremely anxiety provoking (score 4). Dental phobics had significantly higher mean scores on all stimuli, including typically B-I-I-related stimuli, than those without dental phobia (all *P* < *0.01*). For both dental phobics and non-dental phobics the stimulus with the highest mean score was "undergoing root canal treatment" (95% CI 3.45–3.86 and 2.27–2.31, respectively). This stimulus was also most frequently reported as extremely anxiety provoking among both groups (73.9%, and 11.0%, respectively). Among dental phobics, it appeared that typical B-I-I-related stimuli had a relatively low ranking among the 28 fears of dental objects and situations, except the stimulus "having surgery," which was ranked third. Of all 28 stimuli dental phobics rated the B-I-I-related stimulus "seeing blood" as lowest. The results for dental phobia were similar to those for dental fear. Individuals with a high level of dental

Table 1. Sociodemographic characteristics of the participants with and without dental phobia, with and without dizziness or fainting during dental treatment, and with and without avoidance of dental care

Variable, % or Mean (±SD)	Dental phobia n = 48	No dental phobia n = 11,165	Wald χ^2 or t	*p*-value	Dizziness or fainting during dental treatment n = 472	No dizziness or fainting during dental treatment n = 10,588	Wald χ^2 or t	*p*-value	Avoidance of dental care n = 2,010	No avoidance of dental care n = 9,114	Wald χ^2 or t	*p*-value
Presence												
Overall	0.4%	99.6%			4.3%	95.7%			18.1%	81.9%		
Male	0.3%	99.7%	2.70	0.10	2.8%	97.2%	35.60	<0.01	22.2%	77.8%	80.42	<0.01
Female	0.5%	99.5%			5.2%	94.8%			15.4%	84.6%		
Age												
Overall	48.45 (±15.59)	44.24 (±17.01)	2.01	0.044	42.37 (±17.52)	44.20 (±17.00)	-2.86	<0.01	45.12 (±27.34)	44.01 (±15.99)	2.51	0.012
Male	50.44 (±11.77)	46.26 (±16.29)	1.38	0.167	46.20 (±15.22)	46.12 (±16.29)	0.07	0.94	46.95 (±28.06)	46.07 (±15.64)	1.38	0.17
Female	47.71 (±16.66)	42.94 (±15.55)	1.81	0.070	41.08 (±17.76)	42.96 (±15.63)	-2.51	0.012	43.44 (±25.41)	42.81 (±14.95)	1.07	0.29
Country of birth												
The Netherlands	100%	97.4%	0.84[1]	0.36[1]	98.3%	97.4%	0.82	0.37	97.2%	7.5%	0.24	0.62
Other country	0.0%	2.6%			1.7%	2.6%			2.7%	2.5%		
Education												
Primary-lower vocational	46.2%	19.7%	15.08	<0.01	19.8%	19.6%	0.01	0.93	26.2%	18.3%	42.82	<0.01
Intermediate-higher vocational-university	53.8.0%	80.3%			80.2%	80.4%			63.8%	81.7%		

[1]Test statistic not produced in STATA, but in SPSS.

Table 2. Rank order (based on mean score), mean scores (and 95% CI) and the proportion of participants with and without dental phobia who rated the stimulus as extremely anxiety provoking (score 4)

	Dental phobics (n = 48)				Non-dental phobics (n = 11,165)					
Stimulus	**Rank order**	**Mean score (1-4)**	**95% CI**	**Proportion of dental phobics rating stimulus as extremely anxiety provoking**	**Rank order**	**Mean score (1-4)**	**95% CI**	**Proportion of non-dental phobics rating stimulus as extremely anxiety provoking**	**t-value**	***p-value***
Undergoing root canal treatment	1	3.65	3.45-3.86	73.9%	1	2.29	2.27-2.31	11.0%	14.53	<0.01
Insufficient anaesthetics	2	3.49	3.24-3.74	66.0%	2	2.23	2.21-2.24	8.9%	10.85	<0.01
Dentist drilling your tooth or molar	3	3.37	3.15-3.59	47.8%	8	1.90	1.88-1.92	2.9%	14.14	<0.01
Having surgery[1]	3	3.37	3.11-3.63	56.5%	3	2.16	2.14-2.18	5.7%	9.74	<0.01
Being pushed about roughly/ harshly	5	3.35	3.12-3.58	50.0%	6	1.98	1.96-1.99	4.2%	12.73	<0.01
Extraction of tooth or molar	6	3.34	3.09-3.59	52.3%	5	2.12	2.10-2.14	6.4%	10.36	<0.01
Cutting or tearing in soft tissue	7	3.28	3.00-3.55	51.1%	4	2.13	2.12-2.15	5.7%	8.55	<0.01
A dentist in a hurry	8	3.17	2.90-3.44	42.6%	7	1.91	1.89-1.93	3.3%	9.79	<0.01
Feeling helpless	9	3.07	2.78-3.35	39.1%	18	1.66	1.64-1.67	2.1%	10.41	<0.01
Pain	10	3.04	2.78-3.29	37.5%	8	1.90	1.89-1.92	3.4%	8.85	<0.01
Things at the back of your mouth	11	2.98	2.69-3.27	37.0%	12	1.81	1.79-1.82	3.0%	8.39	<0.01
The fact that you don't know what is going to happen	12	2.93	2.64-3.23	34.8%	18	1.66	1.64-1.67	1.3%	8.97	<0.01
Not knowing what's happening in your mouth	13	2.91	2.64-3.18	27.7%	21	1.54	1.53-1.56	1.3%	10.51	<0.01
The sound of the drill	13	2.91	2.64-3.19	30.4%	17	1.68	1.67-1.70	2.0%	9.21	<0.01
Objects in your mouth	15	2.85	2.54-3.15	32.6%	22	1.48	1.47-1.50	1.0%	9.26	<0.01
A cavity in a tooth or molar being filled	16	2.81	2.51-3.12	29.2%	22	1.51	1.50-1.53	1.2%	8.71	<0.01
Receiving an injection[1]	17	2.79	2.43-3.15	40.0%	14	1.78	1.77-1.80	3.1%	5.73	<0.01
Being injured[1]	18	2.76	2.45-3.07	30.4%	13	1.79	1.78-1.81	2.1%	6.41	<0.01

Table 2. Rank order (based on mean score), mean scores (and 95% CI) and the proportion of participants with and without dental phobia who rated the stimulus as extremely anxiety provoking (score 4) (*continued*)

	Dental phobics (n = 48)				Non-dental phobics (n = 11,165)					
Stimulus	**Rank order**	**Mean score (1-4)**	**95% CI**	**Proportion of dental phobics rating stimulus as extremely anxiety provoking**	**Rank order**	**Mean score (1-4)**	**95% CI**	**Proportion of non-dental phobics rating stimulus as extremely anxiety provoking**	**t-value**	***p-value***
A sense of vomiting	19	2.73	2.38-3.08	39.6%	10	1.85	1.84-1.87	3.6%	5.54	<0.01
Gagging	20	2.72	2.38-3.07	38.3%	15	1.75	1.73-1.77	3.2%	5.83	<0.01
Fainting	20	2.72	2.37-3.08	36.2%	10	1.85	1.84-1.87	5.3%	5.04	<0.01
An unpleasant remark made by de dentist	22	2.67	2.37-2.98	26.1%	20	1.56	1.54-1.57	2.8%	7.56	<0.01
Seeing sharp dental instruments	23	2.61	2.32-2.96	19.6%	25	1.37	1.36-1.39	0.4%	8.87	<0.01
Lack of explanation by the dentist	24	2.60	2.29-2.91	20.0%	16	1.69	1.68-1.71	1.8%	5.96	<0.01
Lying in the dental chair (position)	25	2.52	2.26-2.78	13.0%	27	1.21	1.20-1.22	0.4%	10.09	<0.01
Braces being fixed to your teeth	26	2.39	2.07-2.71	19.6%	24	1.44	1.43-1.46	0.9%	6.00	<0.01
Feeling numb	27	2.15	1.85-2.45	13.0%	27	1.21	1.20-1.21	0.1%	6.42	<0.01
Seeing blood[1]	28	2.04	1.72-2.37	12.8%	26	1.26	1.25-1.27	0.8%	4.91	<0.01

[1] B-I-I related stimulus

fear, but without fulfilling all screening criteria of dental phobia (*n* = 573), had significantly higher mean scores on all stimuli than those with a relatively low level of dental fear (all *P* < 0.01). Moreover, regarding the rank order of typical B-I-I-related stimuli, "having surgery" was ranked third, "receiving an injection" 16th, "being injured" 17th, and "seeing blood" 28th.

Overlap between dental phobia and a history of fainting during dental treatment

Of the dental phobics, 13.0% (*n* = 6) reported a history of fainting during dental treatment (Fig. 1). Dental phobics were significantly more likely (OR = 3.4; (95% CI: 1.5–8.1) to report a history of fainting than non-dental phobics [Wald χ^2 (1) = 7.68; *P* < 0.01]. Of the individuals with a high level of dental fear, but without fulfilling all screening criteria of dental phobia, 17.8% (*n* = 101) reported a history of fainting (Fig. 1). They were significantly more likely (OR = 6.0; 95% CI: 4.7–7.6) to report a history of fainting than individuals without a high level of dental fear [Wald χ^2 (1) = 204.71; *P* < 0.01].

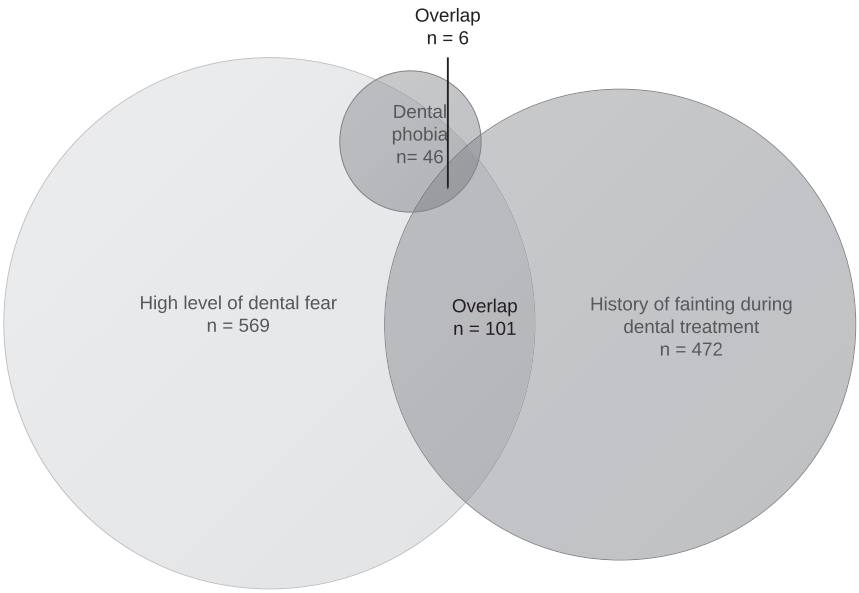

Figure 1. Overlap between dental phobia and a history of fainting during dental treatment and a high level of dental fear and a history of fainting during dental treatment

Avoidance of dental care

Table 3 shows the proportion of participants that reported a tendency to avoid dental care and the associations with other variables. Avoidance of dental care was found to be significantly more likely among dental phobics than among those without dental phobia (OR

Table 3. Strength of the associations between the independent variables and avoidance of dental care.

Participants	Avoidance of dental care					
	% avoiders	*N*	Wald χ^2	OR	95 % CI	*p*-value
Gender						
Female	15.4%	1,052	80.42	0.6	0.6-0.7	<0.01
Male	22.2%	956				
Education						
Intermediate-higher vocational-university	16.3%	1,051	42.82	0.6	0.6-0.7	<0.01
Lower vocational	23.6%	373				
Dental phobia						
Yes	52.1%	25	30.53	5.0	2.8-8.8	<0.01
no	17.9%	1,985				
High level of dental fear						
Yes	30.6%	175	68.05	2.3	1.9-2.7	<0.01
No	16.6%	1,709				
Fainting history during dental treatment						
Yes	18.0%	85	0.030	1.0	0.8 – 1.2	0.86
No	17.7%	1,869				
Extreme fear of having surgery						
Yes	21.9%	141	8.08	1.3	1.1-1.6	<0.01
No	17.4%	1,773				
Extreme fear of receiving an injection						
Yes	22.5%	81	6.04	1.4	1.1-1.8	0.014
No	17.5%	1,885				
Extreme fear of getting injured						
Yes	21.9%	51	3.07	1.3	1.0-1.8	0.080
No	17.5%	1,789				
Extreme fear of the sight of blood						
Yes	27.2%	25	5.68	1.8	1.1-2.8	0.017
No	17.5%	1,904				
Extreme fear of fainting						
Yes	19.1%	109	0.97	1.1	0.9 – 1.4	0.33
No	17.5%	1,723				

= 5.0; 95% CI: 2.8–8.8). A similar relationship was found for dental fear (OR = 2.3; 95% CI: 1.9–2.7). However, a history of fainting during dental treatment was not found to be related to avoidance of dental care (OR = 1.0; 95% CI: 0.8–1.2).

Discussion

This is the first study that investigated the co-occurrence of dental phobia, B-I-I-related fears, and vasovagal fainting in a large population-based sample. The results show that dental phobics fear B-I-I-related objects and situations (e.g. seeing blood), although they fear other stimuli present in dental setting (e.g. undergoing root canal treatment) more. These findings are consistent with earlier findings that showed that patients with dental phobia or dental fear demonstrate a high level of fear of multiple stimuli, particularly involving invasive procedures (e.g. root canal treatment procedures and extractions), but not of blood, injury, or injections per se (Oosterink et al., 2008; De Jongh et al., 1998; De Jongh et al., 1995; Kleinknecht et al., 1973).

Although presence of dental phobia was significantly associated with fainting during dental treatment, only a minor proportion of the dental phobics reported a history of fainting when exposed to their stimulus situation (i.e. a dental treatment). This corroborates previous reports on the small overlap between individuals with high levels of dental fear and fainting (De Jongh et al., 1998; Locker et al., 1997), and is far less than the percentage of 75% reported in patients with B-I-I phobia according to the DSM-IV-TR (APA, 2000). It is also in line with previous studies which showed that none of the dental phobics experienced fainting (De Jongh et al., 1998), and none displayed a biphasic response pattern, when exposed to their phobic stimuli (Leutgeb et al., 2011). In previous studies with dental phobics only heart rate acceleration was observed (Elsesser et al., 2006; Sarlo et al., 2002; Fredrikson, 1981), a response pattern contrary to the biphasic response pattern, which is described as being the core phenomenon of B-I-I phobia (APA, 2000). On the other hand, despite the fact that only a minority of the dental phobics reported a fainting response, they were found to be three times more likely to have experienced such a response during dental treatment than those who did not fulfill the criteria of dental phobia. An explanation for this finding might be that a part of the dental phobics also suffer from a B-I-I-specific phobia subtype, such as blood phobia, apart from their dental phobia (De Jongh et al., 1998; Starcevic & Bogojevic, 1997).

Another important question is whether the alleged biphasic response pattern of dental phobia translates into avoidance of necessary care, and therefore may exert detrimental effects on dental health (APA, 2000). It was indeed found that, besides being male and having a low level of education, the presence of dental phobia and its less pathological variant, dental fear, was significantly associated with greater avoidance of dental care. However, the present study failed to find support for the hypothesis that fainting is significantly associated with avoidance of dental care. Thus, dental phobia, and not a vasovagal fainting tendency, seems to be a risk factor of avoidance of proper care, and accordingly, for deteriorating dental health. The present findings are in line with the only other study that examined the

relationship between fainting and avoidance of dental care (Vika et al., 2008), which showed that fear was an explanatory factor for avoidance of dental treatment, whereas a fainting experience during a dental injection was not.

Some limitations of the study need to be mentioned. Firstly, although the self-report checklist used to identify individuals with dental phobia has been validated against a structured diagnostic interview (i.e. SCID; First & Gibbon, 2004) it is possible that cases were missed. Therefore, it is important to replicate the findings in a large clinical sample. Also, the number of individuals meeting the criteria of dental phobia in the present sample was relatively small (0.4%), and much lower than previously found in a large representative sample of the Dutch population (3.7%; Oosterink et al., 2009). A possible explanation for this difference is that the current study used a written invitation with a request to fill out a web-based survey, which may have provided individuals with dental phobia the opportunity to avoid participating. This is in contrast with the study of Oosterink et al. (2009) that used face-to-face administration to collect data. Given the response rate of 40.2%, we cannot exclude a nonresponse bias related to dental phobia. However, previous studies addressing nonresponse in the Netherlands Twin Registry related to a variety of traits, showed that the effects of nonresponse bias are unlikely to be large (Vink et al., 2004). Another explanation for the low prevalence of dental phobia found is the relatively high level of education in this sample (Statistics Netherlands, 2012) since dental fear and dental phobia have been found to be less prevalent in highly educated people than in lower educated people (Armfield et al., 2006). However, since our results using another operationalization of pathological dental fear (i.e. DAS ≥ 13) showed virtually the same results, it is unlikely that this low prevalence of dental phobia limits the conclusions of the present study. Finally, in order to determine whether fainting would be associated with avoidance of dental care, we classified respondents as having a tendency to avoid dental care when they indicated that they visited a dentist less than once a year during the past 5 years. Clearly, there are many more reasons why people do not visit a dentist on an annual basis than anxiety per se, such as lack of access to care, or financial reasons. However, given the high SES of the sample, such reasons may be less likely. Maybe more relevant to note is that we were not able to tease out clinically relevant or clinically meaningful (i.e. pathological) forms of avoidance.

The results of the present study challenge the current classification of dental phobia as a subtype of B-I-I phobia for several reasons. First, the results show that dental phobics demonstrate fear of multiple stimuli, including the sound of the dental drill, and having insufficient anesthesia, but not of blood, injury, or injections per se (Oosterink et al., 2008; De Jongh et al., 1995). The finding that a significant proportion of the dental phobics endorsed having surgery (56%) and receiving injections (40%) as highly anxiety provoking is not a justification for its current classification, but might best be explained as the result of associative learning (i.e. classical conditioning). Many common situations in the dental

setting are invasive in its nature (e.g. drilling, anesthetic injections, endodontic treatments, surgical procedures such as surgical removal of wisdom teeth) that could easily elicit pain and, consequently, a fear response. In this way, patients learn to associate previously neutral stimuli (e.g. the dental chair, the sound of the drill, and dental instruments) with the experience of pain by which the dental context becomes a conditioned response to a danger signal that has predictive value in this potentially harmful situation. Secondly, with regard to the vasovagal response pattern of dental phobics, this study showed that only a minority of dental phobics also suffers from a tendency to faint. These findings add to existing evidence against a model in which dental phobia is considered to be part of the B-I-I phobia subtype (Leutgeb et al., 2011; Schmid-Leuz et al., 2007; Elsesser et al., 2006; De Jongh et al., 1998; Locker et al., 1997). It is however not a surprise that dental phobia is in some way related to B-I-I phobia, since B-I-I-related stimuli (e.g. injections or blood) are inevitable aspects of the dental setting. There are many more examples of separate syndromes that appear similar in the dental setting of which the disease processes differ in etiology, including the person with claustrophobia who fears not being able to escape from the dental treatment room. However, having this fear does not imply that this person should be considered as suffering from dental phobia.

Given that dental phobia does not fit in the remaining specific phobia subtypes (i.e. the animal, situational, or natural environment specific phobia subtypes), in the light of recommendations for a next edition of the DSM it may be most appropriate to nosologically classify dental phobia as a specific phobia of the "other category" of specific phobias, a category that already includes other, "oral-related" specific phobia subtypes (e.g. emetophobia and choking phobia; APA, 2000).

Conclusion

The present findings add to existing evidence, and converge on the conclusion, that dental phobia has to be considered a specific phobia subtype independent of the B-I-I subtype within DSM. Further, dizziness and fainting do not seem to play a role in avoidance of dental care.

References

Agras, S.W., Sylvester, D. & Oliveau, D. (1969). The epidemiology of common fears and phobias. Comprehensive Psychiatry, 10: 439–447.

American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. (DSM-IV-TR). Washington, DC; 2000.

Armfield, J.M., Spencer, A.J. & Stewart, J.F. (2006). Dental fear in Australia: who's afraid of the dentist? Australian Dental Journal, 51: 78–85.

Ayala, E.S., Meuret, A.E. & Ritz, T. (2009). Treatments for blood-injury-injection phobia: a critical review of current evidence. Journal of Psychiatric Research, 43: 1235–1242.

Bienvenu, O.J. & Eaton, W.W. (1998). The epidemiology of blood-injection-injury phobia. Psychological Medicine, 28: 1129–1136.

Boomsma, D.I., de Geus, E.J., Vink, J.M., et al. (2006). Netherlands twin register: from twins to twin families. Twin Research and Human Genetics, 9: 849–857.

Burstein, M., Georgiades, K., He, J.P., et al. (2012). Specific phobia among U.S. adolescents: phenomenology and typology. Depression and Anxiety, 29: 1072–1082.

Corah, N.L. (1969). Development of a dental anxiety scale. Journal of Dental Research, 48: 596.

Corah, N.L., Gale, E.N. & Illig, S.J. (1978). Assessment of a dental anxiety scale. Journal of the American Dental Association (1939), 97: 816–819.

Craske, M.G., Barlow, D.H., Clark, D.M., et al. (1996). Specific (simple) phobia. In: Widiger TA, Frances AJ, Pincus HA, Ross R, First MB, Davis WW, editors. DSM-IV Sourcebook, Vol. 2. Washington, DC: American Psychiatric Press; 1996: 473–506.

De Jongh, A., Oosterink, F.M., Kieffer, J.M., Hoogstraten, J. & Aartman, I.H.A. (2011). The structure of common fears: comparing three different models. The American Journal of Psychology, 124: 141–149.

De Jongh, A., Bongaarts, G., Vermeule, I., Visser, K., de Vos, P. & Makkes, P. (1998). Blood-injury-injection phobia and dental phobia. Behaviour Research and Therapy, 36: 971–982.

De Jongh, A., Adair, P. & Meijerink-Anderson, M. (2005). Clinical management of dental anxiety: what works for whom? International Dental Journal, 55: 73–80.

De Jongh, A., Muris, P., Schoenmakers, N. & ter Horst, G. (1995). Negative cognitions and dental phobics: reliability and validity of the dental cognitions questionnaire. Behaviour Research and Therapy, 33: 507–515.

Elsesser, K., Heuschen, I., Pundt, I. & Sartory, G. (2006). Attentional bias and evoked heart-rate response in specific phobia. Cognition and Emotion, 20:1 092–1107.

First, M.B. & Gibbon, M. The structured clinical interview for DSM-IV axis I disorders (SCID-I) and the structured clinical interview for DSM-IV axis II disorders (SCID-II). In: Segal DL, Hilsenroth MJ, Hersen M, editors. Comprehensive Handbook of Psychological Assessment, Vol 2: Personality Assessment. Hoboken, NJ: John Wiley and Sons Inc.; 2004;134–143.

Fredrikson, M., Annas, P., Fischer, H. & Wik, G. (1996). Gender and age differences in the prevalence of specific fears and phobias. Behaviour Research and Therapy, 34: 33–39.

Fredrikson M. (1981). Orienting and defensive reactions to phobic and conditioned fear stimuli in phobics and normals. Psychophysiology, 18: 456–465.

Hamilton, J.G. (1995). Needle phobia: a neglected diagnosis. The Journal of Family Practice, 41: 169–175.

Johnsen, B.H., Thayer, J.F., Laberg, J.C., Wormnes, B., Raadal, M., Skaret, E., Kvale, G. & Berg, E. (2003). Attentional and physiological characteristics of patients with dental anxiety. Journal of Anxiety Disorders 17: 75–87.

Kleinknecht, R.A. & Lenz J. (1989). Blood/injury fear, fainting and avoidance of medically related situations: a family correspondence study. Behaviour Research and Therapy, 27: 537–545.

Kleinknecht, R.A., Klepac, R.K. & Alexander, L.D. (1973). Origins and characteristics of dental fear. Journal of the American Dental Association (1939), 86: 842–848.

Kozak, M.J. & Montgomery, G.K. (1981). Multi modal behavioural treatment for recurrent injury-scene-elicited fainting (vasodepressor syncope). Behavioural and Cognitive Psychotherapy, 9: 316–332.

LeBeau, R.T., Glenn, D., Liao, B., Wittchen, H.U., Beesdo-Baum, K., Ollendick, T. & Craske, M.G. (2010). Specific phobia: a review of DSM-IV specific phobia and preliminary recommendations for DSM-V. Depression and Anxiety, 27:148–167.

Leutgeb, V., Schäfer, A. & Schienle, A. (2011). Late cortical positivity and cardiac responsitivity in female dental phobics when exposed to phobia-relevant pictures. International Journal of Psychophysiology, 79: 410–416.

Locker, D., Shapiro, D. & Liddell, A. (1997). Overlap between dental anxiety and blood-injury fears: psychological characteristics and response to dental treatment. Behaviour Research and Therapy, 35:583–590.

Lundgren, J., Berggren, U. & Carlsson, S.G. (2001). Psychophysiological reactions in dental phobic patients during video stimulation. European Journal of Oral Sciences, 109: 172–177.

Marks, I. (1988). Blood-injury phobia: a review. American Journal of Psychiatry, 145: 1207–1213.

Mulder, M. (RIVM). Contact met tandarts 2005–2008. Volksgezondheid Toekomst Verkenning, Nationale Atlas Volksgezondheid. Bilthoven: RIVM, <http://www.zorgatlas.nl> Zorgatlas\Zorg\Eerstelijnszorg\Mondzorg, 2010.

Neale, M.C., Walters, E.E., Eaves, L.J., Kessler, R.C., Heath, A.C. & Kendler, K.S. (1994). Genetics of blood-injury fears and phobias: a population-based twin study. American Journal of Medical Genetics, 54: 326–334.

Oosterink, F.M.D., De Jongh, A., Hoogstraten, J. (2009). Prevalence of dental fear and phobia relative to other fears and phobia subtypes. European Journal of Oral Sciences, 117:135–143.

Oosterink, F.M.D., De Jongh, A., Aartman, I.H.A. (2008). What are people afraid of during dental treatment? Anxiety-provoking capacity of 67 stimuli characteristic of the dental setting. European Journal of Oral Sciences, 116: 44–51.

Öst, L.G., Sterner, U. & Lindhahl, I.L. (1984). Psychological responses to blood phobics. Behaviour Research and Therapy, 22: 109–117.

Öst, L.G. (1992). Blood and injection phobia: background and cognitive, physiological, and behavioral variables. Journal of Abnormal Psychology, 101: 68–74.

Öst, L.G., Fellenius, J. & Sterner, U. (1991). Applied tension, exposure in vivo, and tension-only in the treatment of blood phobia. Behaviour Research and Therapy, 29: 561–574.

Page, A.C. (1994). Blood-injury phobia. Clinical Psychology Review, 14: 443–461.

Page, A.C. & Martin, N.G. (1998). Testing a genetic structure of blood-injury-injection fears. American Journal of Medical Genetics Part B: Neuropsychiatric Genetics 81: 377–384.

Sarlo, M., Palomba, D., Angrilli, A. & Stegagno, L. (2002). Blood phobia and spider phobia: two specific phobias with different autonomic cardiac modulations. Biological Psychology, 60:91–108.

Schmid-Leuz, B., Elsesser, K., Lohrmann, T., Jöhren, P. & Sartory, G. (2007). Attention focusing versus distraction during exposure in dental phobia. Behaviour Research and Therapy, 45: 2691–2703.

Starcevic, V. & Bogojevic, G. (1997). Comorbidity of panic disorder with agoraphobia and specific phobia: relationship with the subtypes of specific phobia. Comprehensive Psychiatry, 38:315–320.

Statistics Netherlands. Beroepsbevolking; behaalde onderwijs naar herkomst geslacht en leeftijd [Working population; educational attainment by ethnicity sex and age]. Voorburg/Heerlen, the Netherlands: Statistics Netherlands; 2012.

Vika, M., Skaret, E., Raadal, M., Ost, L.G., Kvale, G. (2008). Fear of blood, injury, and injections, and its relationship to dental anxiety and probability of avoiding dental treatment among 18-year-olds in Norway. International Journal of Paediatric Dentistry, 18:163–169.

Vink, J.M., Willemsen, G., Stubbe, J.H., et al. (2004). Estimating non-response bias in family studies: application to mental health and lifestyle. European Journal of Epidemiology, 19:623–630.

Willemsen, G., Vink, J.M., Abdellaoui, A., et al. (2013). The adult Netherlands twin register: 25 years of survey and biological data collection. Twin Research and Human Genetics, 16:271–281.

I’m not extremely afraid of the dental treatment, but I can’t stop gagging with all the instruments in my mouth. Therefore it is not possible to fill my teeth properly. I don’t know why I need to gag, but I feel ashamed towards the dentist and I feel sad, because my teeth deteriorate.

CHAPTER 7

Self-reported gagging in dentistry: prevalence, psycho-social correlates and oral health

C.M.H.H. van Houtem, A.J. van Wijk, D.I. Boomsma,
L. Ligthart, C.M. Visscher, A. de Jongh

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Introduction

The tendency to gag during dental treatment or even during tooth brushing can be debilitating and severely limit both the patient's ability to accept good quality dental care and the clinician's ability to deliver it. Yet, gagging is a relatively unexplored area in dental research. For example, reliable estimates of its prevalence and socio-demographic correlates in the general population are completely lacking.

There are indications that individuals who suffer from an excessive gag reflex are more anxious about the dental treatment than those without (Randall et al., 2014; Akarslan & Erten, 2010), but the relationship of gagging with other psychological variables (e.g. specific fears of stimuli involving the dental setting, anxious depression or underlying general personality traits, such as neuroticism) is largely unknown.

As gagging is considered to be a negative experience (Armfield, 2010), it is conceivable that specific dental stimuli that trigger a gag reflex could easily become aversive stimuli leading to avoidance behavior (Hainsworth et al., 2008), with negative consequences for oral health (Bassi et al., 2004). However, besides one effort (Akarslan & Yildirim Biçer, 2013), the relation of gagging with dental attendance and oral health has hardly been investigated.

The purpose of this study was to bridge the gap in the existing information about gagging during dental treatment. The first aim of this study was to derive a prevalence estimate of gagging during dental treatment in a large sample based on patient-reported information. The second aim was to investigate some socio-demographic (i.e. gender, age, country of birth and level of education) and psychological (i.e. dental trait anxiety, fear of dental objects and situations, anxious depression and neuroticism) correlates of gagging and the relationship between patients' self-report of gagging and oral health (i.e. having untreated cavities, bleeding of the gingiva and wearing full dentures), and avoidance of dental care. Finally, it was determined which combination of variables was most strongly related to gagging during dental treatment.

Methods

Data collection and participants

Data were collected among twin families registered with the Netherlands Twin Register (NTR; Willemsen et al., 2013). Adult NTR participants (N = 27,892) received a written invitation to participate in the survey. From this group, 11,948 individuals completed the questionnaire (response rate 42.8%; see for a detailed description of the data collection and sample Ligthart *et al*. (2014)). Six individuals were excluded because they were younger than 18 years and 171 because they did not complete the question about gagging during

dental treatment. This resulted in a sample of 11,771 individuals from 5,277 families for analysis with a mean age (±sd) of 44.39 (±15.67) years (age range 18.12–100.43 year), and with 61.8% being female.

Measures

Self-reported gagging during dental treatment

The tendency to gag during dental treatment was assessed with the question 'Do you tend to gag during dental treatment? (yes/no)'.

Socio-demographic variables

The survey included questions about sex and age. Based on previous questionnaires (Willemsen et al., 2013), information on country of birth was available for 10,781 individuals (91.6%) and level of education was available for 8,500 individuals (72.2%). These variables were dichotomized into the Netherlands versus other, and primary-low versus intermediate-high.

Psychological variables

Dental trait anxiety

Severity of dental trait anxiety was assessed with the Dental Anxiety Scale (DAS; Corah, 1969). Responses are scored from 1 to 5, providing total scores ranging from 4 (not anxious at all) to 20 (extremely anxious). Dental Anxiety Scale scores of 13 or higher are considered indicative of the presence of a high level of dental fear (Corah et al., 1978). Internal consistency reliability (Cronbach's alpha) in this study was 0.90. The test–retest reliability of the DAS in a Dutch sample was 0.80 (intra-class correlation coefficient; Stouthard, 1989). The DAS was chosen to assess dental trait anxiety because it is the most widely used questionnaire to assess dental anxiety; however, one critical review suggests that the validity of the DAS should be considered moderate (Schuurs & Hoogstraten, 1993).

Fear of stimuli comprising the dental setting

To assess fear of objects and situations related to the dental setting, a questionnaire with 25 stimuli was used. These 25 stimuli were the most prevalent among 67 stimuli found in a previous study (Oosterink et al., 2008). This questionnaire was supplemented with three additional stimuli (i.e. gagging, a sense of vomiting and fainting). The fear-provoking nature of each item was scored on a four-point scale, from 1 ('not at all fear provoking') to 4 ('extremely fear provoking'). Each of the variables was dichotomized into 'not or not extremely fear provoking' versus 'extremely fear provoking'.

Anxious depression

To index symptoms of anxiety and depression, the DSM-IV-oriented subscale for anxiety and depressive problems of the Adult Self Report (ASR; Achenbach, Bernstein & Dumenci, 2005; Achenbach & Rescorla, 2003) was used, consisting of 18 items. The responses are scored on a three-point scale (0 = not true, 1 = somewhat or sometimes true, 2 = very true or often true), providing total scores ranging from 0 to 36 and reflecting a quantitative measure of anxious depression. Higher scores indicate more symptoms of anxious depression (Achenbach, Bernstein & Dumenci, 2005). Internal consistency reliability (Cronbach's alpha) in this study was 0.90. The test–retest reliability of the subscale for anxiety and depression is 0.87 ($P < 0.01$; Achenbach & Rescorla, 2003). The ASR has demonstrated good content validity, criterion-related validity and construct validity (Achenbach et al., 2005), which was confirmed in two Dutch studies (Ferdinand et al., 1995; Ferdinand & Verhulst, 1995).

Neuroticism

Neuroticism was assessed using the neuroticism subscale of the NEO Five Factor Inventory (NEO-FFI; Costa & McCrae, 1992). The neuroticism subscale consists of twelve items. Responses are scored from 1 to 5, providing total scores ranging from 12 to 60. This questionnaire has been completed previously (Willemsen et al., 2013), and therefore, information was available for 9,453 individuals. Internal consistency reliability (Cronbach's alpha) is 0.87. The test–retest reliability of the neuroticism subscale of the NEO-FFI is 0.89 (Robins et al., 2001). The validity of the neuroticism subscale is good (Hoekstra et al., 1996).

Self-reported oral health

Presence of cavities

Presence of cavities was assessed using a question about self-reported health state of teeth. For this study, this variable was dichotomized into 'I have no cavities' versus 'I have few/many cavities'.

Presence of gingival bleeding

Presence of gingival bleeding was assessed using a question about bleeding of the gingiva during tooth brushing. This variable was dichotomized into 'my gums never bleed/my gums used to bleed, but they don't anymore' versus 'my gums bleed occasionally or often'.

Presence of complete dentures

Whether someone had complete dentures was assessed with the following question: 'Do you still have one or more of your own teeth or molars?' with 'yes' or 'no, I have a complete set of false teeth' as possible answers.

Avoidance of dental care

In the Netherlands, regular dental attendance is described as the proportion of people who visit the dentist at least once a year (Mulder, 2010). Individuals who reported to visit the dentist, dental hygienist or preventive assistant for a check-up and/or treatment once in a year or more during a five-year period were classified as regular attendees. Those visiting the dental care professional less than once a year during a five-year period were classified as avoiders of care.

Statistical analyses

First, descriptive statistics were obtained using IBM SPSS Statistics version 20. Linear (continuous measures) and logistic regression (categorical measures) analyses were produced using STATA 12.1. STATA's robust cluster option was used to allow for the non-independence of family members. Univariate associations between patients' self-report of gagging during dental treatment on the one hand and socio-demographic variables, psychological variables, self-reported oral health and avoidance of dental care on the other were estimated by calculating odds ratios for categorical measures, or unstandardized regression coefficients (B) and their 95% confidence intervals (95% CI) for continuous measures. Next, multiple logistic regression analysis, with patients' self-report of gagging during dental treatment as a dependent variable and all variables reported in Tables 1 and 2 as independent variables, was used to determine which combination of variables was associated with gagging during dental treatment. For all statistical analyses, a *P*-value < 0.05 was considered statistically significant.

Results

Prevalence and socio-demographic characteristics

Table 1 presents data on the estimated prevalence of gagging and socio-demographic characteristics of individuals with and without gagging during dental treatment. Overall, 8.2% (95% CI 7.7–8.7) of the participants (*n* = 970) reported to gag during dental treatment. Women were significantly more likely to gag than men, in general, and in the age groups of 18–24 and 35–64 years, but not in the age group of 25–34 and ≥65 years. Participants who reported to gag had a significantly higher mean age and were more likely to have a lower level of education than those who did not report gagging during dental treatment.

Psychological variables

Participants who indicated to gag during dental treatment scored significantly higher on all psychological variables, including dental trait anxiety, anxious depression and neuroticism,

Table 1. Prevalence, socio-demographic characteristics, psychological variables, self-reported oral health and avoidance of dental care in individuals with and without gagging during dental treatment

Variable	Gagging		No gagging					
Prevalence of gagging	**N**	**Proportion**	**N**	**Proportion**	**Wald χ^2**	**OR**	**95% CI**	***p-value***
Overall	970	8.2%	10,801	91.8%				
Male	285	6.3%	4,216	93.7%				
Female	685	9.4%	6,585	90.6%	33.61	1.54	1.33 – 1.78	<0.001
By age group								
18-24 years	135	6.2%	2034	93.8%				
Male	32	4.2%	726	95.8%				
Female	103	7.3%	1308	92.7%	7.62	1.79	1.18 – 2.70	0.006
25-34 years	109	7.4%	1373	92.6%				
Male	29	6.2%	441	93.8%				
Female	80	7.8%	932	92.1%	1.34	1.31	0.83 – 2.05	0.25
35-44 years	188	8.0%	2149	92.0%				
Male	56	6.5%	810	93.5%				
Female	132	9.0%	1339	91.0%	4.39	1.43	1.02 – 1.99	0.036
45-54 years	233	10.0%	2095	90.0%				
Male	48	6.0%	747	94.0%				
Female	185	12.1%	1348	87.9%	20.16	2.14	1.53 – 2.97	<0.001
55-64 years	200	9.6%	2083	90.4%				
Male	75	7.2%	965	92.8%				
Female	145	11.5%	1118	88.5%	12.00	1.67	1.25 – 2.23	<0.001
≥65 years	85	7.4%	1067	92.6%				
Male	45	7.9%	527	92.1%				
Female	40	6.9%	540	93.1%	0.39	0.87	0.56 – 1.35	0.53
Sociodemographic characteristics								
Mean age (years ± SD)	970	46.02 (14.94)	10,801	44.24 (15.73)	12.05	1.78	0.77-2.78	<0.001
Male	285	48.73 (15.69)	4,216	46.12 (16.10)	7.47	2.61	0.74-4.48	0.006
Female	685	44.90 (14.48)	6,585	43.03 (15.37)	9.53	1.86	0.68-3.04	0.002
Country of birth	881		9,900					
Other country	17	1.9%	208	2.1%				
The Netherlands	864	98.1%	9.692	97.9%	0.12	0.92	0.56 – 1.50	0.73
Education level	742		7,758					
Primary-Low	178	24.0%	1,551	20.0				
Intermediate-High	564	76.0%	6,207	80.0	6.83	0.79	0.66 – 0.94	0.009
Psychological variables								
Dental trait anxiety (DAS 4 -20)								
Overall	955	9.32 (3.46)	10,617	7.29 (2.59)	299.04	2.03	1.80-2.25	<0.001
Male	277	8.46 (3.23)	4,143	6.64 (2.19)	84.62	1.82	1.43-2.21	<0.001
Female	678	9.67 (3.48)	6,474	7.71 (2.74)	193.59	1.96	1.68-2.23	<0.001

Table 1. Prevalence, socio-demographic characteristics, psychological variables, self-reported oral health and avoidance of dental care in individuals with and without gagging during dental treatment (*continued*)

Variable	Gagging		No gagging					
Anxious depression (0 - 30)								
Overall	956	5.19 (5.84)	10,618	4.31 (5.16)	19.54	0.87	0.49-1.26	<0.001
Male	281	4.15 (5.27)	4,144	3.29 (4.53)	6.87	0.86	0.22-1.50	0.009
Female	675	5.62 (6.01)	6,474	4.97 (5.42)	7.16	0.65	0.17-1.13	0.008
Neuroticism (12 – 60)								
Overall	803	30.39 (7.71)	8,650	28.85 (7.39)	28.83	1.54	0.98-2.10	<0.001
Male	226	28.03 (7.65)	3,149	26.51 (6.84)	8.33	1.51	0.49-2.55	0.004
Female	577	31.31 (7.53)	5,501	30.19 (7.36)	11.31	1.12	0.47-1.78	0.001
Self-reported oral health								
State of teeth	912		10,352					
No cavities	805	88.3%	9,467	91.5%				
A few/many untreated cavities	107	11.7%	885	8.5%	10.37	1.42	1.15 – 1.76	0.0013
Bleeding of the gingiva	909		10,371					
Never	582	64.0%	7,497	72.3%				
Occasionally or often	327	36.0%	2,874	27.7%	26.83	1.47	1.27 – 1.69	<0.001
Complete dentures	966		11,180					
No	911	94.3%	10,780	96.3%				
Yes	55	5.7%	400	3.7%	9.34	1.57	1.17 – 2.09	0.0022
Avoidance of dental care	965		10,772					
No	777	80.5%	8,821	81.9%				
Yes	188	19.5%	1,951	18.1%	1.12	1.09	0.93 – 1.29	0.29

compared with non-gagging participants (Table 1). Furthermore, the gagging participants (16.4%) were significantly more likely to report a high level of dental trait anxiety (i.e. DAS ≥ 13) compared with the non-gagging participants (4.6%; OR = 4.12; 95% CI 3.39–5.01; $P < 0.001$). Table 2 presents data on the proportion of individuals with an extreme fear of stimuli comprising the dental setting. For all 28 stimuli, a significant greater proportion of gagging individuals reported these stimuli as extremely anxiety provoking compared to non-gagging individuals (ORs ranging from 2.08 to 11.47). The highest ORs were found for extreme fears of typical gagging-related stimuli, such as objects in the back of the mouth.

Table 2. Proportions of individuals with an extreme fear of anxiety provoking stimuli in individuals with and without gagging during dental treatment

	Gagging		No gagging				
Stimulus	**N**	**Proportion**	**N**	**Proportion**	**Wald χ^2***	**OR**	**95% CI**
Having a root canal treatment	212	23.1%	1037	10.1%	130.94	2.68	2.26 – 3.17
Things at the back of your mouth	155	16.5%	206	2.0%	409.91	9.88	7.92 – 12.34
Insufficient anaesthetics	154	16.4%	901	8.6%	59.98	2.08	1.73 – 2.51
Having surgery	144	15.1%	543	5.2%	131.00	3.29	2.68 – 4.03
Extractions of tooth or molar	137	14.5%	626	5.9%	94.53	2.69	2.20 – 3.29
Gagging	129	13.6%	241	2.3%	268.67	6.57	5.25 – 8.23
The sense of vomiting	128	13.6%	286	2.8%	229.29	5.53	4.43 – 6.90
Being pushed about/rough/ harsh	120	12.9%	387	3.7%	147.86	3.84	3.09 – 4.78
Cutting or tearing in soft tissue	109	11.6%	573	5.5%	52.93	2.26	1.81 – 2.81
Fainting	97	10.6%	509	5.0%	48.02	2.25	1.79 – 2.83
A dentist in a hurry	78	8.4%	321	3.1%	62.20	2.87	2.21 – 3.74
Dentist drilling your tooth or molar	79	8.3%	274	2.6%	85.86	3.42	2.64 – 4.44
Receiving an injection	73	7.6%	312	2.9%	58.18	2.74	2.12 – 3.56
Objects in your mouth	65	7.0%	68	0.6%	192.15	11.47	8.12 – 16.19
A remark made by de dentist	63	6.7%	192	1.8%	81.06	3.85	2.87 – 5.15
Pain	63	6.6%	345	3.3%	27.12	2.10	1.59 – 2.78
Feeling helpless	57	6.1%	198	1.9%	61.01	3.37	2.48 – 4.56
Lack of explanation of the dentist	48	5.2%	173	1.7%	49.15	3.24	2.33– 4.50
Getting injured	47	5.2%	198	1.9%	38.12	2.78	2.01 – 3.84
The fact that you don't know what is going to happen	47	5.0%	122	1.2%	73.40	4.52	3.20 – 6.38
The sound of the drill	47	5.0%	187	1.8%	42.10	2.94	2.12 – 4.06
Not knowing what's happening in the mouth	41	4.3%	123	1.2%	54.19	3.86	2.70 - 5.54
Filling of a cavity in a tooth or molar	38	4.0%	108	1.00%	52.24	4.04	2.77- 5.90
Braces fixed on your teeth	29	3.3%	83	0.8%	41.71	4.08	2.66 – 6.24
Lying in the dental chair (position)	21	2.2%	32	0.3%	50.52	7.47	4.29 – 13.00
Sight of certain dental instruments	20	2.1%	37	0.3%	40.71	6.14	3.52 – 10.73
The sight of blood	18	1.9%	82	0.8%	11.96	2.48	1.48 – 4.14
Feeling numb	8	0.8%	15	0.1%	16.63	6.00	2.54 – 14.19

*All *ps* < 0.001

Self-reported oral health

Participants who reported to gag during dental treatment were significantly more likely to report untreated cavities, gingival bleeding during tooth brushing and the wearing of complete dentures compared with those without such a tendency (Table 1).

Avoidance of dental care

No difference in avoidance of dental care could be detected between individuals who indicated to gag and those who indicated not to gag during treatment. Also, no significant interaction between dental trait anxiety and gagging was found in relation to avoidance of dental care (OR = 1.16; 95% CI 0.76–1.33; Wald χ^2 (1) = 0.47; P = 0.50).

Logistic regression analyses

All variables of Tables 1 and 2 were entered as predictors into a multiple logistic regression model. Table 3 shows the results of the final multiple regression model, in which only significant predictors were retained. The model was statistically significant [Wald χ^2 (39) = 255.85; P < 0.001; Nagelkerke R^2 = 0.076], with ten predictors significantly contributing to the prediction.

Table 3. Odds ratios for significant predictor variables in logistic regression model predicting gagging during dental treatment

	Odds ratio	95% CI	*p- value*
Female	1.56	1.22 – 1.98	<0.001
High level of dental trait anxiety	1.97	1.23 – 3.15	0.004
Bleeding of the gingiva	1.36	1.09 – 1.71	0.007
Extreme fear of			
Things at the back of your mouth	3.77	2.17 – 6.53	<0.001
The sight of blood	3.17	1.04 – 9.61	0.042
Objects in your mouth	2.49	1.11 – 5.58	0.027
Having a root canal treatment	1.47	1.00 – 2.15	0.050
Cutting or tearing in soft tissue	0.59	0.36 – 0.99	0.045
Fainting	0.48	0.26 – 0.91	0.025
Not knowing what's happening in the mouth	0.24	0.066 – 0.90	0.034

Discussion

As far as we know, this study provides a first population-based estimate of dental treatment-related self-reported gagging. Overall, more than eight percent of the participants reported to gag, with higher prevalence reports among women compared to men, and among

individuals with a lower level of education. The estimated prevalence of gagging seems to incline with increasing age, with the highest prevalence reports among individuals between 45 and 54 years.

Gagging individuals reported higher levels of dental trait anxiety than non-gagging individuals. This is consistent with several other studies (Randall et al., 2014; Uziel et al., 2012; Winocur et al., 2011; Akarslan & Erten, 2010). In addition, patients' self-report of gagging was more strongly associated with severity of a number of specific gagging-related fears (e.g. objects in the mouth or things at the back of the mouth) than with typical dental fears (e.g. fear of the dental drill, or other common stimuli comprising the dental setting). This is in line with the *classical conditioning theory* (Davey, 1997), which predicts that when an initially neutral (*conditioned*) stimulus (CS; e.g. an object in the back of the mouth) has once been paired with a negative experience (i.e. gagging; *unconditioned stimulus, US*), which elicited a (*unconditioned*) fear response (UR), the latter can become a learned (i.e. *conditioned*) response (CR) to cues which more or less *predict* the occurrence of unconditioned response (US; gagging) for which the individual prepares by a fear response (CR).

It is assumed that feelings of embarrassment associated with gagging (Hainsworth et al., 2008) might discourage patients from seeking dental care, resulting in a deteriorating oral health (Bassi et al., 2004). Indeed, gagging individuals reported a worse oral health condition, and significantly more of them indicated wearing full dentures, than their non-gagging counterparts. Surprisingly, however, in the present study, no difference in dental attendance pattern was found between both groups. Although in agreement with findings of Akarslan and Yildrim Biçer (2013), this finding is inconsistent with what the *operant conditioning theory* would predict [i.e. behaviour patterns increase in frequency because these ensure sympathy and attention (positive reinforcement) or lead to avoidance (negative reinforcement)]. Possibly, although gagging does not lead to irregular attendance, the oral health condition of gagging individuals is negatively affected by the fact that they are less able to provide themselves with proper oral care, and that dental care professionals are less able to offer adequate dental care.

A combination of variables, including sex, dental trait anxiety, fear of particularly gagging-related stimuli and gingival bleeding, maximized the prediction of dental-related gagging. However, the combination of all potential predictive variables explained only a modest part of the variance of dental-related gagging. This finding suggests that a variety of other, local, systemical, anatomical, iatrogenic, idiosyncratic (e.g. exposure to certain life events that increase sensitivity of the gag reflex), and biological (e.g. genetic) factors are likely to play a role as well.

A number of limitations need to be noted. Firstly, the cross-sectional nature of the study limits inferences with causality. To this end, it remains unclear whether the elevated levels of dental trait anxiety are the cause, or the result, of peoples' tendency to gag dur-

ing dental treatment. Secondly, oral health was assessed with self-reported oral health measures. Although self-reports have been found to correlate with objectively established clinical features (Pitiphat et al., 2002), these data are certainly less accurate than when an intra-oral examination would have been used. Thirdly, gagging was assessed using a single dichotomous question, since at the time of sending the first wave of questionnaires (January 2011), no valid or reliable Dutch version of such an instrument was available that was appropriate for research as a self-assessment instrument of gagging during dental treatment. However, gagging is not necessarily a dichotomous phenomenon and the use of one yes/no self-reported question might not have been a sufficient way to evaluate this complex issue. Furthermore, there was a lack of data regarding age of onset, etiology and severity of the gag reflex both inside and outside the dental setting. Therefore, albeit the findings of the current study should be interpreted with caution, these are valuable in providing clues for future research regarding dental treatment-related gagging, and associations with a wide set of variables. As the data of the current study were derived from a large number of twin families of the Netherlands Twin Register (NTR; Willemsen et al., 2013) not only population-based conclusions can be drawn, in the future familial prevalence or heritability of dental treatment-related gagging may become available.

In conclusion, the results of the present study suggest that people who report gagging are moderately dentally anxious, fear-specific situations that can trigger a gagging response and, in spite of visiting the dentist equally frequently, have a worse self-reported oral health than those who do not gag. Given the fact that only a part of the variance was explained by socio-demographic and psychological variables, it remains important to conduct studies that include a much broader set of variables than has been done until now. In other words, to gain a better understanding of the causes, maintenance and treatment of this complex, both intriguing and debilitating, phenomenon, studying the interaction of psychological, social and biological factors is pivotal.

References

Achenbach, T.M. & Rescorla, L.A. (2003). Manual for the ASEBA adult forms & profiles. Burlington,VT: University of Vermont, Research Center for Children, Youth & Families.

Achenbach, T.M., Bernstein, A. & Dumenci, L. (2005). DSM-oriented scales and statistically based syndromes for ages 18 to 59: linking taxonomic paradigms to facilitate multitaxonomic approaches. Journal of Personality Assessment, 84: 49–63.

Akarslan, Z.Z. & Erten, H. (2010). Reliability and validity of the Turkish version of the shorter form of the gagging problem assessment questionnaire. Journal of Oral Rehabilitation, 37: 21–25.

Akarslan, Z.Z. & Yildirim Biçer, A.Z. (2013). Influence of gag reflex on dental attendance, dental anxiety, self-reported temporomandibular disorders and prosthetic restorations. Journal of Oral Rehabilitation, 40: 932–939.

Armfield, J.M. (2010). Towards a better understanding of dental anxiety and fear: cognitions vs. experiences. European Journal of Oral Sciences, 118: 259–264.

Bassi, G.S., Humphris, G.M. & Longman, L.P. (2004). The etiology and management of gagging: a review of the literature. Journal of Prosthetic Dentistry, 91: 459–467.

Corah, N.L. (1969). Development of a dental anxiety scale. Journal of Dental Research, 48: 596.

Corah, N.L., Gale, E.N. & Illig, S.J. (1978). Assessment of a dental anxiety scale. Journal of the American Dental Association (1939), 97: 816–819.

Costa, P.T. & McCrae, R.R. (1992). Revised NEO Personality Inventory (NEO-PI-R) and NEO Five-Factor Inventory (NEO-FFI); Professional Manual. Odessa, FL: Psychological Assessment Resources.

Davey, G.C.L. (1997). A conditioning model of phobias. In: Davey GCL, ed. Phobias, a handbook of theory, research and treatment. Chichester, UK: Wiley:301–322.

Ferdinand, R.F., van der Reijden, M., Verhulst, F.C., Nienhuis, F.J. & Giel, R. (1995). Assessment of the prevalence of psychiatric disorder in young adults. British Journal of Psychiatry, 166: 480-488.

Ferdinand, R.F. & Verhulst, F.C. (1995). Psychopathology in Dutch young adults: enduring or changeable? Social Psychiatry and Psychiatric Epidemiology, 30: 60–64.

Hainsworth, J.M., Hill, K.B., Rice, A. & Fairbrother, K.J. (2008). Psychosocial characteristics of adults who experience difficulties with retching. Journal of Dentistry, 36:494–499.

Hoekstra, H.A., Ormel, J. & deFruyt F. (1996). Handleiding NEO persoonlijkheidsvragenlijsten NEO-PI-R en NEO-FFI. Lisse: Swets Test Services.

Ligthart, L., Visscher, C.M., van Houtem, C.M.H.H., Geels, L.M., Vink, J.M. & De Jongh, A. (2014). Pain symptoms in a Dutch population sample: relationship with sex, age and anxious depression. The Journal of Pain, 15:945–955.

Mulder, M., RIVM. Contact met tandarts 2005–2008. Volksgezondheid Toekomst Verkenning, Nationale Atlas Volksgezondheid. Bilthoven: RIVM; 2010. http://www.zorgatlas.nl.Zorgatlas\Zorg\Eerstelijnszorg\Mondzorg.

Oosterink, F.M.D., De Jongh, A. & Aartman, I.H.A. (2008). What are people afraid of during dental treatment? Anxiety-provoking capacity of 67 stimuli characteristic of the dental setting. European Journal of Oral Sciences, 116:44–51.

Pitiphat, W., Garcia, R.I., Douglass, C.W. & Joshipura, K.J. (2002). Validation of self-reported oral health measures. Journal of Public Health Dentistry, 62:122–128.

Randall, C.L., Shulman, G.P., Crout, R.J. & McNeil, D.W. (2014). Gagging and its associations with dental care-related fear, fear of pain and beliefs about treatment. Journal of the American Dental Association (1939), 145:452–458.

Robins, R.W., Fraley, R.C., Roberts, B.W. & Trzesniewski, K.H. (2001). A longitudinal study of personality change in young adulthood. Journal of Personality, 69: 617–640.

Schuurs, A.H. & Hoogstraten, J. (1993). Appraisal of dental anxiety and fear questionnaires: a review. Community Dentistry and Oral Epidemiology, 2: 329–339.

Stouthard, M. (1989). Angst voor tandheelkundige behandelingen, Thesis, Amsterdam: University of Amsterdam.

Uziel, N., Bronner, G., Elran, E. & Eli I. (2012). Sexual correlates of gagging and dental anxiety. Community Dental Health. 29: 243–247.

Willemsen, G., Vink, J.M., Abdellaoui, A., den Braber, A., van Beek, J.H.D.A., Draisma, H.H.M. et al. (2013). The adult Netherlands twin register: twenty-five years of survey and biological data collection. Twin Research and Human Genetics, 16: 271–281.

Winocur, E., Uziel, N., Lisha, T., Goldsmith, C. & Eli, I. (2011). Self-reported Bruxism – associations with perceived stress, motivation for control, dental anxiety and gagging. Journal of Oral Rehabilitation, 38: 3–11.

CHAPTER 8

Summary and general discussion

The main aim of this thesis was to increase the knowledge about a set of conditions and behaviours that potentially limit treatment of dental patients in clinical practice, i.e., dental anxiety, dental phobia, gagging and fainting during dental treatment. The second aim was to find an answer to the question as to whether or not these difficulties are interrelated or should be considered as separate entities. Therefore, the following topics were studied: 1) heritability estimates of specific phobias and corresponding fears (*Chapter 2)*; 2) the conceptual structure of dental fear *(Chapter 3);* 3) the etiology and maintenance of dental trait anxiety and dental phobia *(Chapter 4 and 5)*; 3) the conceptual validity of dental phobia as a subtype of the blood-injection-injury phobia *(Chapter 6)*; and 4) the psychosocial correlates (including dental anxiety) of gagging *(Chapter 7)*.

This final chapter firstly provides a brief chapter-by-chapter summary of the studies presented in this thesis.

Summary "Anxiety, fainting and gagging in dentistry – Separate or overlapping constructs?"

Evidence from twin studies suggests that genetic factors contribute to the risk of developing a fear or a phobia. The purpose of the study presented in *Chapter 2* was to review the current literature regarding twin studies describing the estimated heritability of specific phobias and their corresponding fears. This was done by a systematic search of the published literature between 1967 and April 2012. After selection, 15 articles were included for review, including ten twin studies on specific phobias and five twin studies on fears. Heritability estimates of both specific phobia and fear subtypes varied widely, even within the subtypes. A meta-analysis performed on the twin study results indicated that specific phobias and fears are moderately heritable. The highest mean heritability (±SEM) among specific phobias was for the blood–injury–injection phobia (33% ± 0.06) and among the fear subtypes this was found for animal fear (45% ± 0.004). For most phobias and fears, variance could be explained merely by additive genetic and unique environmental effects, while the influence of common environmental effects appeared to be modest or absent. However, since the relatively low number of studies conducted in the field of specific phobias and fears, additional research is needed to further explore the complex etiology of specific phobia and fear subtypes.

Dental fear is a very broad concept, and dentally fearful patients can display more or less fear of different dentally related stimuli. As such, it has been argued that dental fear should not be considered a homogeneous construct (Oosterink et al., 2008). Because there is limited empirical information as to whether or how the different types of stimuli associ-

ated with dental fear relate to one another, the purpose of the study presented in *Chapter 3* was to develop a descriptive framework for the classification of dental fear. Data were collected using an online and offline survey among Dutch twin families (n = 11,717), consisting of adult twins, their spouses, their parents and/or other family members. Firstly, the entire sample was randomly divided into two subsamples of respectively 5,920 and 5,851 individuals. Next, on the first subsample an exploratory factor analysis (EFA) was performed to determine the factor structure of a set of in total 28 potentially dental fear provoking objects and situations. The second sample was used to confirm the newly derived factor structure by means of confirmatory factor analysis (CFA). The EFA yielded a 3-factor solution with 70.7% explained variance pertaining to: fear of (1) invasive treatment; (2) lack of self-control; and (3) physical sensations. The CFA showed an acceptable fit to the data, thereby confirming the stability of the earlier identified 3-factor structure.

Since knowledge about memories of distressing events underlying fears and specific phobias in general, and more specifically dental fear and phobia, is limited, in *Chapter 4* a study is presented that was aimed to assess the presence, content, and characteristics of memories of events that initiated or exacerbated dental anxiety levels using a semi-structured interview. Also the relationship between dental trait anxiety and some key features of these memories were investigated. Individuals with dental phobia (n = 42), with subthreshold dental phobia (i.e., having extremely high levels of dental trait anxiety, but without fulfilling all screening criteria for dental phobia; n = 41), and normal controls (i.e., having average levels of dental trait anxiety; n = 70) were included as participants in the study. Dental phobics were more likely to report at least one memory underlying their anxiety than the normal controls. Moreover, dental phobics' memories were reported as more vivid, disturbing, and more intensely relived than the memories of the normal controls. Greater severity of dental trait anxiety was significantly associated with greater disturbance of patients' memories.

From laboratory studies, it is known that distressing, aversive situations that trigger an adrenal (stress) response can enhance emotional memory formation. However, examples of translational research replicating these findings in clinical relevant situations, e.g. with fearful dental patients exposed to an invasive dental treatment, are limited. The study presented in *Chapter 5* aimed to examine how core characteristics of emotionality ('vividness' and 'disturbance') of a memory of an invasive dental treatment change over a two-week period. It was hypothesized that (1) memories of individuals with severe dental anxiety would be significantly more vivid and disturbing than memories of their low anxious counterparts, immediately after the event and two weeks later, and (2) that memory characteristics of this event would be associated with the level of anxiety experienced during this event. The study used a subsample of the clinical sample of the study presented in *Chapter 4,* consisting of 47 severely, and 67 low, dentally anxious patients. After two weeks, in both groups a significant

decline in memory vividness was observed. In contrast, the disturbance of the memory of the anxious individuals increased significantly, and remained stable in the reference group. State anxiety during dental treatment significantly predicted vividness ($r = 0.46$, $p < 0.001$) and disturbance ($r = 0.55$, $p < 0.001$) of the memory of this treatment two weeks later.

In *Chapter 6,* the results of a study that investigated the conceptual validity of dental phobia, as being part of the Blood-Injection-Injury (B-I-I) phobia within DSM-IV-TR (APA, 2000), are presented. The purpose of the study was to determine the co-occurrence of dental phobia, typical dental (and B-I-I related) fears, vasovagal fainting, and avoidance of dental care. Data for this study were collected by an online survey among Dutch twin families (n = 11,213). The results showed that individuals with a positive screen of dental phobia rated typical B-I-I-related stimuli as relatively little anxiety provoking. Presence of dental phobia appeared to be significantly associated with a history of dizziness or fainting during dental treatment (OR = 3.4; 95% CI: 1.5–8.1), but of the dental phobic individuals only 13.0% reported a history of dizziness or fainting during dental treatment.

In *Chapter 7* an attempt was made to bridge some gaps in the existing knowledge about gagging during dental treatment. Although gagging has a profound effect on the delivery of dental care, it is still a relatively under-investigated and poorly understood phenomenon. Data used in the study were collected with a survey among Dutch twin families (n = 11,771). Estimated overall prevalence of gagging during dental treatment was 8.2% (95% CI 7.7–8.7). Patients' self-report of gagging was found to be significantly associated with being female, a lower level of education and higher levels of dental trait anxiety, gagging-related fears (e.g., fear of objects in the mouth), anxious depression and neuroticism. Gagging also appeared to be significantly associated with self-reported untreated cavities, gingival bleeding and wearing full dentures, but not with avoidance of dental care. It can be concluded that individuals who report to gag during dental treatment are most likely to be moderately dentally anxious and fear specific situations that can trigger a gagging response. Although those who reported to gag during dental treatment reported to visit the dentist equally frequently, they reported to have a poorer oral health compared to those who did not report to gag.

General discussion

In the paragraphs below the most important findings are discussed, largely following the build-up of the chapters of this dissertation. Further, some practical and theoretical implications are given, as well as suggestions for future research. Furthermore, in this discussion an attempt is made to explain the overlap between dental anxiety and other anxiety disorders, as well as the overlap between dental anxiety, fainting and gagging during dental treatment.

A genetic liability to develop (dental) anxiety

In *Chapter 2* an overview of twin studies reporting the heritability estimates of specific phobias and fears was presented. The results add weight to our understanding of the etiology of specific phobias and fears in providing information about how much of the individual variation in the liability to specific phobias and fears in a particular population at a certain time is due to genetic influences (Rutter & Plomin, 1997). In general, it was concluded that variance of specific phobias and corresponding fears could be explained by additive genetic and individual specific effects. Only one other study provided heritability estimates of dental anxiety in an adult population (Vassend et al., 2011), suggesting that dental anxiety is moderately heritable. Clearly, additional research that examines the heritability of dental anxiety is warranted. Initially, this was one of our aims, but as already mentioned in the introduction of this thesis, for several reasons it appeared to be not feasible to perform twin analyses and to estimate the heritability of dental anxiety.

For the oral health professional and the individual patient the clinical relevance of the findings of the study presented in *Chapter 2* is limited. The results do not help us to determine, for an individual patient, to which extent his or her fear or phobia is genetically determined, and to what extent these conditions are environmentally determined (Sullivan et al., 2000; Rutter & Plomin, 1997). Therefore, it is impossible to translate population based heritability estimates, such as the estimated heritability of dental anxiety, directly to the fearful patient. Clinicians can only inform their patients that a proportion of their patients' anxiety is "due to genes", but that the environment, for instance the dental setting, that potentially promotes exposure to disturbing and/or arousing experiences, is critically important for the development of anxiety (Sullivan et al., 2000; Merikangas & Risch, 2003).

Emotional memory formation and (dental) anxiety

It is a known fact that distressing and arousing experiences in general enhance emotional memory formation (e.g., Mueller & Cahill, 2010) by activating the amygdala (e.g., McGaugh, 2004). However, across individuals, large differences in the strength of emotional memories exist (see *Chapter 4 and Chapter 5*). These individual differences in emotionality of the memories as well as their ability to vividly recall, are associated with vulnerability to, and maintenance of, anxiety disorders, including specific phobias (Haas & Canli, 2008; Lonergan et al., 2013). The findings of the study presented in *Chapter 4,* that assessed the presence and content of emotional memories associated with dental anxiety, suggests that exposure to a distressing (dental) event, and the way the memory is subsequently stored, was an important conditioning factor for dental anxiety. The presence of a memory of a disturbing

dental event among individuals with either low or pathological levels of dental anxiety or dental phobia was commonly observed. However, large differences were found between those with high and low levels of dental anxiety regarding some emotional characteristics of their memories. For instance, almost two-third of the memories of the dental phobics showed characteristics of Posttraumatic Stress Disorder (PTSD; i.e., intrusiveness and avoidance propensity) compared to only 8% of the memories of the low anxious controls, indicating a larger mental burden of disease in dental phobics compared with normal controls.

The study presented in *Chapter 5* shows that highly anxious individuals reported to have a more vivid and disturbing memory of a recent invasive dental treatment. The question arises why some individuals have highly emotional memories and subsequently develop pathological levels of dental anxiety after exposure to a disturbing (dental) event, while others do not. It could be argued that, besides a specific event, such as exposure to a distressing dental treatment, internal, individual specific, risk factors play a crucial role in the onset and development of anxiety (Mineka & Oehlberg, 2007). Evidence suggests that 'neuroticism' is an example of such an internal risk factor. Neuroticism is an underlying personality trait that has been found to be about 50% heritable and purported to be related to most anxiety disorders (Middeldorp et al., 2005; Hettema et al., 2006). Furthermore, neuroticism has been found to be a genetic vulnerability factor for fear and anxiety disorders (Hettema et al., 2006), which may be systematically related to individual variation in abnormal associative fear learning, emotional memory formation and memory recall, and in turn, to the pathogenesis of fear and anxiety disorders (Haas & Canli, 2008; McGaugh, 2004). To this end, certain genetic variations, such as a polymorphism of the ADRA2b gene, have been found to be associated with enhanced emotional memory formation (Li et al., 2015; Todd et al., 2011; De Quervain et al., 2007). Future research should investigate whether genetic variations that have been found to be associated with differences in responsiveness to acute stress and the subsequent storage of emotionally charged memories of dental events, would also be capable of explaining severity of dental trait anxiety. To investigate whether highly anxious individuals more often possess the polymorphism of ADRA2B gene compared with low anxious individuals, DNA samples were collected, from most of the participants presented in *Chapter 4 and 5*. Unfortunately, as already mentioned in the introduction of this thesis, the majority of the first set of samples that were analysed did not contain enough DNA to perform DNA-analysis.

Although a better understanding of genetic contributions to human memory formation has huge implications for the understanding of normal and pathological memory (Todd et al., 2011), it should be noted that single genetic variants associated with a complex phenotype (e.g., specific phobia) contribute only a fraction of the phenotypic variance (Goodwin, 2015). For future research a promising development are the so called genome wide association studies (GWAS), testing about 2 million genetic loci at a time. Although these studies already

have conformed small effects on psychiatric disorders, the sample sizes used currently are too small to detect meaningful results for anxiety (Goodwin, 2015). Thus, although developments in genetic research give us promising ways forward to get more understanding of the development and maintenance of anxiety disorders, the translation of these findings to the clinical setting is a long way off.

Comorbidity between dental anxiety and other psychiatric disorders

Another point that needs to be stressed here is the comorbidity between pathological levels of dental anxiety and other mood and anxiety disorders, often observed in patients visiting dental fear clinics (Pohjola et al., 2011; Locker et al., 2001; Aartman et al., 1997; Roy-Byrne et al., 1994). In general, comorbidity within anxiety disorders, and between anxiety disorders and depression is a common phenomenon (e.g., Goodwin 2015; Boschloo et al., 2015; Middeldorp et al., 2005;) and in genetic epidemiological studies explained by shared genetic vulnerability (Middeldorp et al., 2005) with neuroticism as underlying personality trait (Middeldorp et al., 2005). Vassend and colleagues (Vassend et al., 2011) demonstrated that neuroticism, assessed with the NEO Personality Inventory Revised (Costa & McCrae, 1992) and dental anxiety, assessed with the Dental Anxiety Scale (Corah, 1969) also shared a proportion (17%) of genetic risk factors (Vassend et al., 2011). Although in this study only a relatively small sample of individuals were included, the results are supported by an increasing body of evidence from heritability studies that suggests that there is substantial overlap between the genetic factors that influence anxiety-related personality traits (neuroticism) and those that increase liability across the anxiety disorders (Smoller et al., 2008; Hettema et al., 2006). Future studies, conducted in larger samples, may give us additional insight in the genetic overlap between pathological forms of dental anxiety and other anxiety disorders.

Related to this, one promising attempt to develop a better understanding of the comorbidity between anxiety disorders, and also of the heterogeneity observed within individuals suffering from the same psychiatric disorder, is the so called *network approach* (Boschloo et al., 2015). This explains individual differences in psychopathology as a result of the interplay between clinical symptoms accompanying these psychiatric disorders. A network structure of 12 psychiatric disorders and 120 psychiatric symptoms was identified, which showed that many symptoms of one psychiatric disorder had indeed strong connections with symptoms of other psychiatric disorders (Boschloo et al., 2015). For instance, the specific phobia symptom “avoidance of specific situation” has been found to have strong connections with the agoraphobia symptom “avoidance of situation because of fear or panic attack” and the panic disorder symptom “unexpected panic attack with at least four symptoms”. Applying such an approach to dental fear and phobia may possibly help us in the future to understand

individual differences in people with pathological forms of dental anxiety, but may also help us to understand and treat complex cases. Namely, greater endorsement of panic symptoms has been found to be associated with higher levels of dental anxiety, more dental avoidance and a worse oral health-related quality of life (Potter et al., 2014). Hence, it can be concluded that psychiatric disorders, including dental anxiety and dental phobia show overlap with other psychiatric disorders, that this overlap can be examined either genetically or clinically, but that it is likely that continuing efforts and research are needed to further unravel the complex network underlying the psychiatric disorders.

In the light of the above issues oral health professionals must take into account that, when treating individuals with pathological forms of dental anxiety, these patients are more likely to have an increased risk of suffering from comorbid anxiety disorders or depressive disorders compared with low anxious patients (Pohjola et al., 2011; Locker et al., 2001; Aartman et al., 1997; Roy-Byrne et al., 1994) which may also complicate the dental treatment (Friedlander & Mahler, 2001; Aartman et al., 1997), or interfere with adequate oral health behaviour at home (Anttila et al., 2006; Friedlander & Mahler, 2001; Friedlander et al., 2002). Therefore, I would recommend, to take, prior to the dental treatment, not only a dental, medical and dental anxiety history, but also take an adequate psychological history. This may help to detect psychopathology that not only may hamper adequate oral health behaviour at home (Friedlander & Mahler, 2001), but also the dental treatment (Aartman et al., 1997) or patient satisfaction about dental treatment, in the case of patients with unexplained dental problems (e.g. severe pain without a clinical observable problem; De Jongh, 2003), or imagined defects in physical appearance following a dental treatment (De Jongh & Adair, 2004).

The heterogeneous nature of dental anxiety

We critically considered the phenomenon “dental anxiety”, since, as previously underlined, dental anxiety is supposed to be a heterogeneous construct encompassing a broad constellation of fears of objects and situations within the dental setting (e.g., Oosterink et al., 2008; De Jongh et al., 1998; Milgrom et al., 1985). The results of our study presented in *Chapter 3,* show three different constructs underlying dental anxiety (i.e., fear of invasive treatment, lack of self-control and physical sensations). However, at this moment, no proper instruments are available that have been found to be capable of assessing these constructs. Currently, questionnaires for the assessment of dental fear and dental anxiety provide only sum scores for dental anxiety levels in general (e.g., the Dental Anxiety Scale, Corah, 1969; the MDAS, Humphris et al., 1995; the S-DAI, Stouthard, 1989; the Dental Fear Survey, Kleinknecht et al., 1984) or do not fully cover all fears present in the dental setting (IDAF-4C+; Armfield, 2010).

Having a sum score for general dental anxiety levels might be of interest for policy makers, for instance, to determine whether or not a fear reducing treatment must be reimbursed. However, these questionnaires have very limited clinical value. Therefore, it needed to to develop and validate questionnaires that properly assess the different subtypes of dental anxiety in order to discriminate between the distinct patient categories, i.e., those who are afraid of (certain aspects of) invasive treatments, those who are afraid of losing control or of physical sensations, since these different patient categories may require different treatment approaches.

The overlap between dental anxiety, dental fainting and dental gagging

Another purpose of this dissertation was to examine whether dental anxiety, fainting and gagging are fully, or partially, overlapping constructs or should be considered as separate entities. The study presented in *Chapter 6* shows that, consistent with our clinical experience and important for the oral health professional, the propensity to faint following a confrontation with a dental or medical stressor is not a characteristic of dental anxiety *per se*, but a distinct condition that can manifest during the dental treatment, affecting approximately 18% of those with high levels of dental anxiety. Unfortunately, in the most recent edition of the DSM, dental phobia is, as other medical phobias, still classified under the heading of blood-injection-injury phobia (APA, 2013), a specific phobia subtype uniquely characterized by a tendency to faint or actual fainting. There is clearly a discrepancy between our findings showing that the only similarity between these phobia subtypes is their relation with a medical environment, and the opinion of the authors who evaluated the diagnostic criteria of specific phobia for the development of DSM-5, and who concluded that "dental phobia shares more similarities than differences with B-I-I phobia" (LeBeau et al., 2010). Accordingly, based upon our findings it may be desirable to reconsider the current description of the B-I-I phobia within the DSM. To this end, we would suggest to change the term "B-I-I phobia" into "medical phobia", since phobia subtypes belonging to the current B-I-I phobia incorporate a wider range of phobias than those directly related to blood, injuries or injections alone. Moreover, since fainting appears not to be a manifestation of fear, but seems more likely to be an innate physiological response in some human individuals when confronted with blood, injuries or injections, the phrase "often characterized by a strong vasovagal response" should be better removed from the text of the DSM.

One of the initial aims of our research was to estimate the heritability of fainting during dental treatment. However, fainting was assessed with a dichotomic measure, which resulted in a considerable loss of information that was demonstrated by the low number of concordant monozygotic (MZ) and dizygotic (DZ) twin pairs who reported to faint during

dental treatment (only 6 of 1061 complete MZ twin pairs and 3 out of 802 complete DZ reported to faint during dental treatment; *unpublished results*). The number of concordant MZ twins exceeded the number of DZ twins, which suggests that fainting during dental treatment has, at least partially, a genetic origin (e.g., van den Berg & Hjelmborg, 2012). However, no further analyses were carried out to estimate the heritability of dental treatment related fainting due to the low number of concordant twins.

The final research chapter of this dissertation (*Chapter 7)* provides data about dental gagging, a relatively unexplored, but clinically highly relevant, area in dental research. In line with the individuals that reported to faint during dental treatment, also the majority of the gagging individuals (about 84%) showed no pathological levels of dental trait anxiety, indicating that dental gagging is a distinct phenomenon that should not be interpreted as symptom of, or as a subtype of, dental trait anxiety or dental phobia. A complicating factor, for both researchers as well as oral health professionals is that gagging patients represent, like patients with dental anxiety, a heterogeneous patient category. For instance, from clinical experience it is known that a part of the gagging patients is not afraid of any aspect of the dental treatment. They feel only embarrassed that, due to their gagging problems, it is difficult to undergo a regular dental treatment. Other people, in contrast, experience severe anxiety of physical sensations associated with gagging, for instance vomiting (see *Chapter 7).* The assessment of dental gagging by means of a standardized assessment instrument has proven to be complicated (Van Linden van den Heuvell et al., 2015). For instance, possible triggers eliciting a gag response seem to be patient specific (Bassi et al., 2004), the frequency and intensity of the gag reflex varies over time, and factors such as the attitude of the dentist (e.g., impatient behaviour) may influence the gag reflex as well (Van Linden van den Heuvell et al., 2015). Finally, gagging can also be a manifestation of underlying psychopathology, for instance, emetophobia (Boschen, 2007). Maybe we must conclude that, despite the huge efforts of various research groups to study dental-treatment related gagging, the development of a reliable assessment instrument for dental gagging is a dead end.

We also aimed to estimate the heritability of the phenomenon of gagging during dental treatment. Since no valid and responsive measures to assess dental treatment related gagging were available, we choose to assess the tendency to gag during dental treatment on a dichotomous scale. Again, like the assessment of dental fainting, the use of a dichotomous scale resulted in a considerable loss of information given the low number of concordant monozygotic (MZ) and dizygotic (DZ) twin pairs reporting to gag during dental treatment. Inspection of our data (*unpublished results*) revealed that the number of concordant MZ twin pairs (31 out of 1061 complete MZ pairs) exceeded the number of concordant DZ twin pairs (7 out of 803 complete pairs) suffering from gagging during dental, indicating, at least partially, a genetic influence (e.g., Van den Berg & Hjelmborg, 2012). Since the number of

complete concordant twin pairs who gag during dental treatment was low, again no further analyses estimating the heritability of gagging could be performed.

For the oral health professional it is important to note that at this moment, although it may be a disappointing message, the etiology of gagging is far from understood, no evidence based treatment to "cure" all different types of dental gagging is available, and the effectiveness of interventions aiming to diminish the gag reflex have not accurately been investigated (Prashanti et al., 2015).

Treatment of patients with severe forms of dental anxiety, fainting and gagging

Figure 1 summarizes the patient categories mentioned in this thesis along with the accompanying treatments for all patient categories referred to in this thesis. In general, the treatment of choice in individuals with severe dental anxiety or dental phobia is a cognitive behavioural treatment approach, aiming to decrease the patients' symptom severity, in combination with the teaching of coping strategies, such as distraction strategies or enhancing patients' sense of self-control. For those suffering from fainting the recommended treatment is applied tension, and for those who gag is, currently, no evidence based treatment available.

General conclusion

Summarizing the paragraphs above, it can be concluded, based on our data and findings of others, that dental treatment-related fainting and gagging are distinct phenomena that should not be interpreted as subtypes of dental fear or dental phobia. Furthermore, perhaps the time has come to completely abandon the terms "dental fear", "dental anxiety" and "dental phobia", given the heterogeneous nature of these conditions, and to classify them according to the fear eliciting stimulus to which it pertains (e.g., the drill, the needle, undergoing surgery), or to the underlying constructs (i.e., fear of invasive treatment, fear of lack of self-control and fear of aversive physical sensations). Either way, it is clear that additional research is warranted to further examine and to better specify the different constructs underlying dental anxiety, gagging and fainting in the dental setting. Furthermore, it is needed to develop, where possible, screening instruments that, after interpreting the results, can guide clinicians to properly assess and treat their patients suffering from fear of (one or more aspects of) the dental treatment situation.

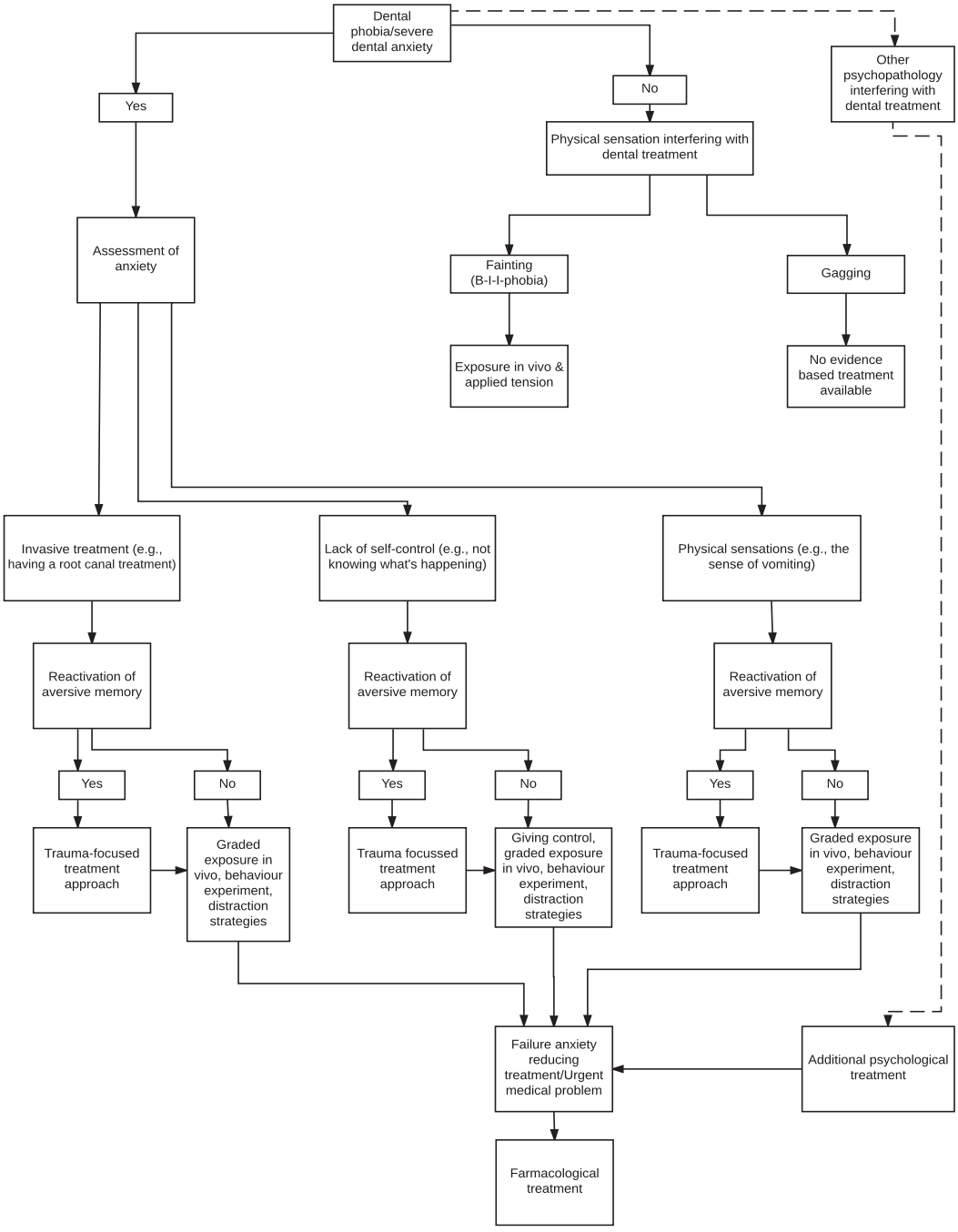

Figure 1. Flowchart of the dental treatment of patients with dental phobia, severe dental anxiety, fainting, gagging and other psychopathology interfering with the dental treatment

References

Aartman, I. H. A., De Jongh, A. & van der Meulen, M. J. (1997). Psychological characteristics of patients applying for treatment in a dental fear clinic. European Journal of Oral Sciences, 105: 384–388.

Airaksinen, E., Larsson, M. & Forsell, Y. (2005). Neuropsychological functions in anxiety disorders in population-based samples: evidence of episodic memory dysfunction. Journal of Psychiatric Research, 39: 207-214.

Airaksinen, E., Larsson, M., Lundberg, I. & Forsell, Y. (2004). Cognitive functions in depressive disorders: evidence from a population-based study. Psychological Medicine, 34: 83–91.

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

Anttila, S., Knuuttila, M., Ylöstalo, P. & Joukamaa, M. (2006). Symptoms of depression and anxiety in relation to dental health behavior and self-perceived dental treatment need. European Journal of Oral Sciences, 114: 109–114.

Armfield, J. & Heaton, L. (2013). Management of fear and anxiety in the dental clinic: a review. Australian Dental Journal, 58: 390–407.

Ayala, E.S., Meuret, A.E. & Ritz, T. (2009). Treatments for blood-injury-injection phobia: a critical review of current evidence. Journal of Psychiatric Research, 43: 1235–1242.

Armfield, J. M. (2010). Development and psychometric evaluation of the Index of Dental Anxiety and Fear (IDAF-4C^{+}). Psychological Assessment, 22: 279-287.

Boschen, M.J. (2007). Reconceptualizing emetophobia: A cognitive–behavioral formulation and research agenda. Journal of Anxiety Disorders, 21, 407-419.

Boschloo, L., van Borkulo, C.D., Rhemtulla, M., Keyes, K.M., Borsboom, D., et al. (2015). The Network Structure of Symptoms of the Diagnostic and Statistical Manual of Mental Disorders. PLoS ONE 10(9): e0137621.

Bracha, H.S. (2004). Freeze, flight, fight, fright, faint: adaptationist perspectives on the acute stress response spectrum. CNS Spectrums, 9: 679-685.

Breslau, N., Davis, G., Peterson, E. & Schultz, L. (1997). Psychiatric sequelae of post-traumatic stress disorder in women. Archives of General Psychiatry, 100: 81-87.

Carter, A.E., Carter, G., Boschen, M., AlShwaimi, E. & George, R. (2014). Pathways of fear and anxiety in dentistry: A review. World Journal of Clinical Cases, 2: 642–653.

Craske, M.G., Treanor, M., Conway, C.C. & Zbozinek, T. (2014). Maximizing exposure therapy: An inhibitory learning approach. Behaviour Research and Therapy, 58: 10–23.

Corah, N. L. (1969). Development of a dental anxiety scale. Journal of Dental Research, 48: 596.

Costa, P. T. & McCrae, R. R. (1992). NEO PI-R professional manual. Odessa, FL: Psychological Assessment Resources.

De Jongh, A., Ernst, R., Marques, L. & Hornsveld, H. (2013). The impact of eye movements and tones on disturbing memories of patients with PTSD and other mental disorders. Journal of Behavior Therapy and Experimental Psychiatry, 44: 447–483.

De Jongh, A., Fransen, J., Oosterink-Wubbe, F. & Aartman, I. (2006). Psychological trauma exposure and trauma symptoms among individuals with high and low levels of dental anxiety. European Journal of Oral Sciences, 114: 286–292.

De Jongh, A., Adair, P. & Meijerink-Anderson, M. (2005). Clinical management of dental anxiety: what works for whom? International Dental Journal, 55: 73–80.

De Jongh, A. (2003). Somatization in dental practice. British Dental Journal, 195: 151-154.

De Jongh, A. & Adair, P. (2004). Mental disorders in dental practice: A case report of Body Dysmorphic Disorder. Special Care in Dentistry, 24: 61-64.

De Jongh, A., Bongaarts, G., Vermeule, I., Visser, K., De Vos, P. & Makkes, P. (1998). Blood-injury-injection phobia and dental phobia. Behaviour Research and Therapy, 36: 971-82.

Friedlander, A.H. & Mahler, M.E. (2001). Major depressive disorder. Psychopathology, medical management and dental implications. Journal of the American Dental Association (1939), 132:629-638.

Friedlander, A.H., Friedlander, I.K. & Marder SR (2002). Bipolar I disorder: psychopathology, medical management and dental implications. Journal of the American Dental Association (1939), 133: 1209-1217.

Fyer, A. J., Mannuzza, S., Chapman, T.F., Martin, L.Y., & Klein, D.F. (1995). Specificity in Familial Aggregation of Phobic Disorders. Arch Gen Psychiatry, 52: 564-573.

Goodwin, G.M. (2015). The overlap between anxiety, depression, and obsessive-compulsive disorder.Dialogues in Clinical Neuroscience, 17: 249-260.

Haas, B. W. & Canli, T. (2008). Emotional memory function, personality structure and psychopathology: A neural system approach to the identification of vulnerability markers. Brain Research Reviews, 58: 71–84.

Hettema, J.M., Neale, M.C. & Kendler, K.S. (2001). A Review and Meta-Analysis of the Genetic Epidemiology of Anxiety Disorders. American Journal of Psychiatry, 158:1568–1578.

Hettema, J.M., Neale, M.C., Myers, J.M., Prescott, C.A. & Kendler, K.S. (2006). A population-based twin study of the relationship between neuroticism and internalizing disorders. American Journal of Psychiatry, 163: 857-864.

Hettema, J.M., Prescott, C.A., Myers, J.M., Neale, M.C. & Kendler, K.S. (2005). The structure of genetic and environmental risk factors for anxiety disorders in men and women. Archives of General Psychiatry, 62: 182-189.

Humphris, G.M., Morrison, T. & Lindsay, S.J.E. (1995). The Modified Dental Anxiety Scale: UK norms and evidence for validity. Community Dental Health, 12: 143-150.

Kessler, R.C., Sonnega, A., Bromet, E., Hughes, M., Nelson, C.B. & Breslau, N. (1999). Epidemiologic risk factors for trauma and PTSD. In: YEHUDA R, ed. Risk factors for post-traumatic stress disorder. Washington, DC: American Psychiatric Association Press,23-59.

Kılıç, C., Ak, S. & Ak, H.B. (2014). Anxiety sensitivity: Another reason to separate dental fears from blood-injury fears? Journal of Anxiety Disorders, 28: 280-282.

Kilpatrick, D.G. & Resnick, H.S. (1992). Post-traumatic stress disorder associated with exposure to criminal victimization in clinical and community populations. In: DAVIDSON JRT, FOA EB, eds. Post-traumatic stress disorder: DSM-IV and beyond. Washington, DC: American Psychiatric Press, 113-143.

Kleinknecht, R.A. (1987). Vasovagal syncope and blood-injury fear. Behaviour Research and Therapy, 25: 175-178.

Kleinknecht, R. A., Thorndike, R. M., McGlynn, F. D. & Harkavy, J. (1984). Factor analysis of the dental fear survey with cross-validation. Journal of the American Dental Association (1939), 108: 59-61.

LeBeau, R. T., Glenn, D., Liao, B., Wittchen, H. U., Beesdo-Baum, K., Ollendick, T., et al.(2010). Specific phobia: a review of DSM-IV specific phobia and preliminary recommendations for DSM-V. Depression and Anxiety, 27: 148–167.

Leutgeb, V., Schafer, A. & Schienle, A. (2011). Late cortical positivity and cardiac responsitivity in female dental phobics when exposed to phobia-relevant pictures. International Journal of Psychophysiology, 79: 410–416.

Li, S., Weerda, R., Milde C., Wolf, O.T. & Thiel, C.M. (2015). ADRA2B genotype differentially modulates stress-induced neural activity in the amygdala and hippocampus during emotional memory retrieval. Psychopharmacology 232: 755–764

Locker, D., Poulton, R. & Thomson, W.M. (2001). Psychological disorders and dental anxiety in a young adult population. Community Dentistry and Oral Epidemiology, 29: 456–463.

Locker, D., Liddell, A., Dempster, L. & Shapiro D. (1999). Age of onset of dental anxiety. Journal of Dental research, 78: 790-796.

Lonergan, M.H., Olivera-Figueroa, L.A., Pitman, R.K. & Brunet, A. (2013). Propranolol's effects on the consolidation and reconsolidation of long-term emotional memory in healthy participants: a meta-analysis. Journal of Psychiatry & Neuroscience, 38: 222–231.

Menzies, R. G. & Clarke, J. C. (1993). The etiology of childhood water phobia. Behaviour Research and Therapy, 31, 499–501.

Menzies, R. G. & Clarke, J. C. (1995). The etiology of phobias: a non-associative account. Clinical Psychology Review, 15, 23–48.

Milgrom, P., Weinstein, P., Kleinknecht, R. & Getz, T. (1985). Treating Fearful Dental Patients. Reston, VA: Reston Publishing Co.

Miller, P. G., Strang, J. & Miller, P. M. (2010). Introduction, in Addiction Research Methods (eds P. G. Miller, J. Strang and P. M. Miller), Wiley-Blackwell, Oxford, UK.

Mueller, D & Cahill, S.P. (2010). Noradrenergic modulation of extinction learning and exposure therapy. Behavioural Brain Research, 208: 1–11.

Mineka, S. & Oehlberg, K. (2008). The relevance of recent developments in classical conditioning to understanding the etiology and maintenance of anxiety disorders, Acta Psychologica, 127: 567-580.

Middeldorp, C.M., Cath, D.C., Van Dyck, R. & Boomsma, D.I. (2005). The co-morbidity of anxiety and depression in the perspective of genetic epidemiology. A review of twin and family studies. Psychological Medicine, 35:611-624.

Oosterink, F. M.D., De Jongh, A. & Aartman, I.H.A. (2008). What are people afraid of during dental treatment? Anxiety-provoking capacity of 67 stimuli characteristic of the dental setting. European Journal of Oral Sciences, 116: 44–51.

Page, A.C. & Martin, N.G. (1998). Testing a genetic structure of blood-injury-injection fears. American Journal of Medical Genetics Part B: Neuropsychiatric Genetics 81: 377–384.

Perkonigg, A., Kessler, R.C., Storz, S. & Wittchen, H.U. (2000). Traumatic events and post-traumatic stress disorder in the community: prevalence, risk factors and comorbidity. Acta Psychiatrica Scandinavica, 101: 46–59.

Pohjola, V., Mattila, A. K., Joukamaa, M. & Lahti, S. (2011). Anxiety and depressive disorders and dental fear among adults in Finland. European Journal of Oral Sciences, 119: 55–60.

Potter, C.M., Kinner, D.G., Tellez, M., Ismail, A.I. & Heimberg, R.G. (2014). Clinical implications of panic symptoms in dental phobia. Journal of Anxiety Disorders, 28: 724-730.

Prashanti, E., Sumanth, K.N., Renjith, G.P., Karanth, L., Soe, H.H.K. (2015). Management of gag reflex for patients undergoing dental treatment. Cochrane Database of Systematic Reviews, 10, Art. No.: CD011116.

McGaugh, J.L. (2004). The amygdala modulates the consolidation of memories of emotionally arousing experiences. Annual Review Neuroscience, 27: 1-28.

Merikangas, K.R. & Risch N. (2003). Will the Genomics Revolution Revolutionize Psychiatry? American Journal of Psychiatry, 160: 625-635.

Roy-Byrne, P.P., Milgrom, P., Khoon-Mei, T., Weinstein, P., Katon, W. (1994). Psychopathology and psychiatric diagnosis in subjects with dental phobia, Journal of Anxiety Disorders, 8: 19-31.

Rutter, M., Plomin, R. (1997). Opportunities for psychiatry from genetic findings. British Journal of Psychiatry, 171: 209–219.

Sarlo, M., Palomba, D., Angrilli, A. & Stegagno, L. (2002). Blood phobia and spider phobia: two specific phobias with different autonomic cardiac modulations. Biological Psychology, 60:91–108.

Seidler, G.H. & Wagner F.E. (2006). Comparing the efficacy of EMDR and trauma-focused cognitive-behavioral therapy in the treatment of PTSD: a meta-analytic study. Psychological Medicine, 36: 1515-1522.

Smoller, J.W., Gardner-Schuster, E. & Covino, J. (2008). The genetic basis of panic and phobic anxiety disorders. American Journal of Medical Genetics, Part C Seminars in Medical Genetics, 148C: 118–126.

Stouthard, M. (1989). Angst voor tandheelkundige behandelingen, Thesis, Amsterdam: University of Amsterdam.

Sullivan, P.F., Neale, M.C. & Kendler, K.S. (2000). Genetic epidemiology of major depression: review and meta-analysis. American Journal of Psychiatry, 157: 1552-1562.

Todd, R.M., Müller, D.J., Palombo, D.J., Robertson, A., Eaton, T., Freeman, N., Levine, B. & Anderson, A.K. (2014). Deletion variant in the ADRA2B gene increases coupling between emotional responses at encoding and later retrieval of emotional memories. Neurobiology of Learning and Memory, 112: 222-229.

Todd, R.M., Palombo, D.J., Brian Levine, B. & Anderson, A.K. (2011). Genetic differences in emotionally enhanced memory. Neuropsychologia, 49: 734-744.

Van den Berg, S. M., & von Bornemann Hjelmborg, J. (2012). Genetic analysis of rare disorders: bayesian estimation of twin concordance rates. Behavior Genetics, 42: 857-65.

Van Linden van den Heuvell, G. F. E. C., de Boer, B., ter Pelkwijk, B. J., Bildt, M. M. & Stegenga, B. (2015). Gagging Problem Assessment: a re-evaluation. Journal of Oral Rehabilitation, 42: 495–502.

Vassend, O., Røysamb, E. & Nielsen, C. S. (2011). Dental anxiety in relation to neuroticism and pain sensitivity. A twin study. Journal of Anxiety Disorders, 25: 302–308.

Weiner, A.A. & Sheehan, D.V. (1990). Etiology of dental anxiety: psychological trauma or CNS chemical imbalance? General Dentistry, 38: 39-43.

SAMENVATTING

Anxiety, fainting and gagging in dentistry - Separate or overlapping constructs?

Deze Nederlandse samenvatting bevat een kort overzicht van de doelen van het proefschrift, de onderzochte onderwerpen en een beknopte samenvatting van de belangrijkste bevindingen van de studies die zijn beschreven in de hoofdstukken twee tot en met zes. Het hoofddoel van dit promotieonderzoek was het vergroten en/of verdiepen van de kennis over extreme tandartsangst, kokhalzen en flauwvallen tijdens de tandheelkundige behandeling. Het tweede doel was te onderzoeken of tandartsangst, kokhalzen en flauwvallen moeten worden beschouwd als elkaar overlappende, of als losstaande fenomenen.

Ten eerste is in *Hoofdstuk 2* een overzicht gegeven van de studies die de geschatte erfelijkheid van specifieke fobieën en hiermee corresponderende angsten beschrijven. Dit is gedaan om beter inzicht te krijgen in de mate waarin specifieke fobieën en angsten, inclusief angst voor de tandheelkundige behandeling, erfelijk zijn. Tandartsangst is een breed begrip, aangezien men voor zeer veel zaken in de tandartspraktijk een angstreactie kan vertonen. Daarom is in *Hoofdstuk 3* de onderliggende structuur van angst voor de tandheelkundige behandeling onderzocht. Het ontstaan van extreme tandartsangst en mechanismen die het in stand houden ervan verklaren zijn onderzocht in *Hoofdstuk 4 en Hoofdstuk 5*. Vervolgens is in *Hoofdstuk 6* de classificering van de tandartsfobie als subtype van de bloed-letsel-injectiefobie(B-L-I-fobie) onderzocht. Het was de vraag was of deze classificatie wel valide was. De B-L-I-fobie onderscheidt zich namelijk van alle andere specifieke fobieën dat mensen die hieraan lijden de neiging hebben tot of daadwerkelijk flauwvallen. Tenslotte is in *Hoofdstuk 7* de associatie tussen kokhalzen en diverse psychosociale variabelen, waaronder angst voor de tandheelkundige behandeling, onderzocht en beschreven.

Samenvatting Hoofdstuk 2: A review and meta-analysis of the heritability of specific phobia subtypes and corresponding fears

In tweelingstudies is aangetoond dat erfelijkheid een rol speelt bij het ontwikkelen van angsten en fobieën. Het doel van de studie in *Hoofdstuk 2* was om een overzicht te geven van de tweelingstudies die de geschatte erfelijkheid van specifieke fobieën en hiermee corresponderende angsten beschrijven. Hiertoe is literatuur onderzocht die is gepubliceerd tussen 1967 en 2012. Uiteindelijk voldeden vijftien artikelen aan alle inclusiecriteria, waarvan tien tweelingstudies over specifieke fobieën en vijf tweelingstudies over angsten. De geschatte erfelijkheid van zowel de specifieke fobieën als de angsten liep wijd uiteen. Uiteindelijk is een meta-analyse uitgevoerd op een subselectie van enkele artikelen. Op basis van deze analyse kan worden geconcludeerd dat specifieke fobieën en angsten matig erfelijk zijn.

De hoogste gemiddelde erfelijkheid (± SEM) bij specifieke fobieën werd gevonden voor de bloed-letsel-injectie fobie (33% ± 0,06). Bij de angsten bleek de angst voor dieren het meest erfelijk te zijn (45% ± 0,004). Verder bleek dat van de meeste fobieën en angsten de variantie volledig kan worden verklaard door genetische en individu-specifieke ervaringen, terwijl de invloed van een gedeelde omgeving zeer klein of afwezig is. Echter, het aantal studies dat is uitgevoerd om de geschatte erfelijkheid van specifieke fobieën en angsten te bepalen is gering. Aanvullend onderzoek is daarom wenselijk om de complexe etiologie van specifieke fobieën en angsten verder te begrijpen en meer inzicht te krijgen in de erfelijkheid van deze aandoeningen.

Samenvatting Hoofdstuk 3: The factor structure of dental fear

Angst voor de tandheelkundige behandeling is geen homogeen begrip, maar een verzamelterm voor een groot aantal angsten voor objecten en situaties die in de tandartspraktijk te vinden zijn, dan wel zich kunnen voordoen (Oosterink et al., 2008). Er is echter weinig empirische informatie beschikbaar óf en zo ja, hoe deze verschillende angsten met elkaar samenhangen. Het doel van het onderzoek in *Hoofdstuk 3* was daarom te bepalen of clusters van object-specifieke en situatie-specifieke angsten ("stimuli") kunnen worden gevonden onderliggend aan het begrip "angst voor de tandheelkundige behandeling". Voor dit onderzoek zijn gegevens verzameld onder volwassenen die zijn ingeschreven bij het Nederlands Tweelingenregister (NTR). De deelnemers werd verzocht een vragenlijst in te vullen en te retourneren. Uiteindelijk stuurden 11.771 deelnemers een vragenlijst retour; een respons van ruim 40%. Vervolgens zijn uit deze respondenten twee willekeurige steekproeven getrokken. Eén van 5.920 en één van 5.851 personen. Op de eerste steekproef is een exploratieve factoranalyse (EFA) uitgevoerd om de factorstructuur van 28 potentieel tandartsangst opwekkende stimuli te bepalen. De tweede steekproef werd gebruikt om de nieuw verkregen factorstructuur via confirmatieve factoranalyse (CFA) te bevestigen. Uit de EFA kwam een drie-factorstructuur naar voren met een verklaarde variantie van 70,7%. De gevonden factorstructuur werd in de CFA bevestigd. De factoren hebben wij als volgt geïnterpreteerd: (1) angst voor invasieve behandelingen (zoals het ondergaan van een wortelkanaalbehandeling), (2) angst voor gebrek aan controle (zoals het niet weten wat er in de mond gebeurt) en (3) angst voor fysieke sensaties (zoals een gevoel van overgeven). De bevindingen van dit onderzoek suggereren dat er ten minste drie verschillende subtypes van angst voor de tandheelkundige behandeling bestaan. Voorts ondersteunen de bevindingen het heterogene karakter van angst voor de tandheelkundige behandeling, hetgeen niet alleen voor onderzoekers van belang is, maar zeker ook voor clinici die werken met angstige patiënten.

Samenvatting Hoofdstuk 4: Presence, content and characteristics of memories of individuals with dental phobia

De kennis over herinneringen aan nare gebeurtenissen die ten grondslag liggen aan angsten en specifieke fobieën is beperkt. In *Hoofdstuk 4* wordt een onderzoek beschreven dat (kenmerken van) herinneringen aan gebeurtenissen beschrijft die volgens de deelnemers ten grondslag lagen aan het ontstaan van hun angst. In dit onderzoek werden patiënten met variërende angstniveaus onderzocht die, ofwel een gespecialiseerde tandarts-angstbegeleiding bezochten vanwege hun angst voor de tandheelkundige behandeling, ofwel een reguliere tandarts. De volgende personen zijn geïnterviewd: 1) 42 patiënten met een fobie voor de tandheelkundige behandeling ("fobici"); 2) 41 patiënten met extreme angst voor de tandheelkundige behandeling, maar zonder tandartsfobie; en 3) 70 patiënten met weinig of geen angst voor de tandheelkundige behandeling ("laagangstigen"). De fobici rapporteerden vaker een herinnering aan een nare gebeurtenis die ten grondslag lag aan hun angst dan de laagangstige patiënten (98% versus 73%). De herinneringen van de fobici waren levendiger, akeliger en intrusiever dan de herinneringen van de laagangstige patiënten en bovendien deden fobici vaker hun best om niet aan de nare ervaring te denken. De herinneringen van de fobici en de extreem angstigen zonder tandartsfobie verschilden niet significant ten aanzien van de levendigheid, de akeligheid en de mate van intrusie. De resultaten suggereren dat herinneringen aan nare gebeurtenissen een belangrijke rol spelen in de ontwikkeling van een fobie voor de tandheelkundige behandeling.

Samenvatting Hoofdstuk 5: Memory characteristics of an arousing event are associated with the level of anxiety during the event: a clinical study among individuals with severe dental anxiety

Uit de literatuur is bekend dat een gebeurtenis waarbij het stress-responssysteem wordt geactiveerd (bijvoorbeeld een nare of akelige gebeurtenis) beter wordt onthouden dan een gebeurtenis waarbij dit niet het geval is. De exploratieve studie beschreven in *Hoofdstuk 5* onderzocht hoe levendig en akelig patiënten zich een invasieve tandheelkundige behandeling (zoals een vulling of een wortelkanaalbehandeling) herinneren. Dit werd aan hen gevraagd zowel meteen na afloop van de behandeling als twee weken later. Een deel van de patiënten dat ook deel had genomen aan het onderzoek beschreven in *Hoofdstuk 4* werd hiervoor benaderd. De hypothese was dat de herinneringen van patiënten met extreme angst voor de tandheelkundige behandeling (n =47), zowel meteen na afloop als twee weken later, levendiger en akeliger zouden zijn vergeleken met de herinneringen van de laagangstige patiënten (n=67). Een tweede hypothese was dat de levendigheid en akeligheid van de herinneringen

zou samenhangen met het door hen zelf gerapporteerde angstniveau tijdens de behandeling. In dit onderzoek hebben wij het zelf gerapporteerde angstniveau tijdens de behandeling beschouwd als een indicator voor activatie van het stress-responssysteem. Meteen na afloop van de behandeling rapporteerden hoogangstige patiënten niet alleen een hoger angstniveau tijdens de behandeling, maar óók dat de behandeling hen levendiger en akeliger voor de geest stond, dan bij de laagangstige patiënten het geval was. Dit gold twee weken later ook nog steeds. Twee weken later was de levendigheid van de herinnering van zowel de hoog- als laagangstige patiënten verminderd. De akeligheid van de herinnering van de hoogangstige patiënten was echter toegenomen, terwijl deze van de laagangstige patiënten gelijk was gebleven. Tenslotte bleek dat het zelf gerapporteerde angstniveau tijdens de tandheelkundige behandeling significant samenhing met de levendigheid ($r = 0,46$, $p < 0,001$) en akeligheid ($r = 0,55$, $p < 0,001$) van de herinnering aan deze behandeling twee weken later. De bevindingen van dit onderzoek geven aanwijzingen voor vervolgonderzoek met als doel te inventariseren of angst voor de tandheelkundige behandeling mogelijk in stand wordt gehouden, doordat bij elke nieuwe tandheelkundige behandeling het stress-responssysteem wordt geactiveerd en de behandeling hierdoor wederom als levendig en akelig wordt onthouden.

Samenvatting Hoofdstuk 6: Is dental phobia a blood-injection-injury phobia?

In de DSM-IV-TR (APA, 2000) is de fobie voor de tandheelkundige behandeling geclassificeerd als subtype van de bloed-letsel-injectiefobie (B-L-I-fobie). De B-L-I-fobie heeft als belangrijkste onderscheidend kenmerk vergeleken met de andere specifieke fobieën dat mensen die hieraan lijden (de neiging hebben tot of echt) flauwvallen, hetgeen bij andere specifieke fobieën niet gebeurt. Bij deze fobieën vertonen mensen bij blootstelling aan een angstwekkende stimulus een stijging van hartslag en bloeddruk, zonder dat deze vervolgens daalt. In *Hoofdstuk 6* is de conceptuele validiteit van de fobie voor de tandheelkundige behandeling als subtype van de bloed-letsel-injectiefobie onderzocht met het oog op de ontwikkeling van de DSM-5 (APA, 2013). Het doel van deze studie was om te onderzoeken in hoeverre de fobie voor de tandheelkundige behandeling, het hebben van angst voor objecten en situaties in de tandheelkundige setting en het flauwvallen bij een tandheelkundige behandeling elkaar overlappen. Gegevensverzameling vond plaats onder volwassenen die zijn ingeschreven bij het Nederlands Tweelingenregister (NTR; $n = 11.213$). De resultaten laten zien dat respondenten met een fobie voor de tandheelkundige behandeling typische B-L-I-gerelateerde stimuli (zoals het zien van bloed) relatief weinig angstwekkend vinden. Het hebben van een fobie voor de tandheelkundige behandeling was significant geassocieerd met een voorgeschiedenis van duizeligheid of flauwvallen tijdens de tandheelkundige behandeling (OR = 3,4; 95% CI: 1,5-8,1). Echter, slechts 13,0% van de tandartsfobici rap-

porteerde een geschiedenis van duizeligheid of flauwvallen tijdens de tandheelkundige behandeling. Dit suggereert dat de overlap tussen het hebben van een fobie voor de tandheelkundige behandeling en het hebben van een B-L-I fobie, minimaal is. Tevens suggereren de resultaten dat een fobie voor de tandheelkundige behandeling en B-L-I moeten worden beschouwd als afzonderlijke aandoeningen. De bevindingen zetten vraagtekens bij de DSM-classificatie “tandartsfobie” als een subtype van de “bloed-letsel-injectiefobie”. Ons advies is dan ook om de huidige tekst van de DSM te herzien.

Samenvatting Hoofdstuk 7: Self-reported gagging in dentistry: prevalence, psycho-social correlates and oral health

Kokhalzen tijdens de tandheelkundige behandeling is een slecht begrepen fenomeen waarnaar relatief weinig gedegen onderzoek is gedaan. Het doel van de studie beschreven in *Hoofdstuk 7* was dan ook enkele lacunes hierover in de bestaande kennis op te vullen. Wederom vond de gegevensverzameling voor deze studie plaats onder volwassenen die zijn ingeschreven bij het Nederlands Tweelingenregister (NTR; 11.771). Aan de respondenten werd gevraagd of zij last hadden van kokhalzen tijdens de tandheelkundige behandeling. De prevalentie van kokhalzen tijdens de tandheelkundige behandeling was 8,2% (95% CI 7,7-8,7). Kokhalzen tijdens de tandheelkundige behandeling bleek, op basis van zelfrapportagedata van de respondenten, significant geassocieerd te zijn met het vrouwelijk geslacht, het hebben van een lager opleidingsniveau, hogere angst voor de tandheelkundige behandeling, aan kokhalzen gerelateerde angsten (bijv. de angst voor voorwerpen in de mond), gevoelens van angst en depressie en de persoonlijkheidstrek “neuroticisme”. Voorts bleek kokhalzen ook significant geassocieerd te zijn met het hebben van onbehandelde gaatjes, bloedend tandvlees en het hebben van een volledige prothese. Daarentegen bleek kokhalzen niet geassocieerd te zijn met het vermijden van tandheelkundige zorg. Slechts 16,4% van de mensen die aangaven te kokhalzen bleek tevens extreem bang voor de tandheelkundige behandeling te zijn. Hieruit kan worden geconcludeerd dat extreme angst voor de tandheelkundige behandeling en het hebben van een verhoogde kokhalsreflex als twee afzonderlijke aandoeningen moeten worden gezien.

Conclusie en suggesties voor vervolgonderzoek

Samenvattend kan op basis van onze data en bevindingen van anderen worden geconcludeerd dat flauwvallen en kokhalzen losstaande fenomenen zijn die niet moeten worden beschouwd als angst voor de tandheelkundige behandeling. Voorts is het, gezien het

heterogene karakter van het verzamelbegrip “angst voor de tandheelkundige behandeling”, aanbevelenswaardig om deze term te laten varen en angst voor de tandheelkundige behandeling bijvoorbeeld te classificeren op grond van de angstwekkende stimulus waar iemand bang voor is (bijvoorbeeld de boor of de verdoving), of één van de door ons gevonden angstcategorieën (angst voor invasieve behandelingen, angst voor een gebrek aan controle en angst voor fysieke sensaties). Vervolgonderzoek kan de door ons geïdentificeerde angstcategorieën verder exploreren en op hun klinische waarde onderzoeken. Een laatste aanbeveling is om, waar mogelijk, meetinstrumenten te ontwikkelen die mondzorgprofessionals kunnen ondersteunen in een adequate diagnostiek en behandeling van hun patiënten die last hebben van angst voor (een of meer aspecten van) de tandheelkundige behandeling.

LIST OF PUBLICATIONS

In this thesis

Houtem, C.M.H.H. van, Laine, M.L., Boomsma, D.I., Ligthart, L., Wijk, A.J., van & De Jongh, A. (2013). A review and meta-analysis of the heritability of specific phobia subtypes and corresponding fears. *Journal of Anxiety Disorders*, 27: 379-388.

[Chapter 2 in this thesis]

Houtem, C.M.H.H. van, Wijk, A.J., van & Jongh, A. de (2015). Presence, content and characteristics of memories of individuals with dental phobia. *Applied Cognitive Psychology*, 29: 515-523.

[Chapter 4 in this thesis]

Houtem, C.M.H.H. van, Aartman, I.H.A., Boomsma, D., Ligthart, L., Visscher, C. & Jongh, A., de (2013). Is dental phobia a blood-injection-injury phobia? *Depression and Anxiety*, 31: 1026–1034.

[Chapter 6 in this thesis]

Houtem, C.M.H.H., van, Wijk, A.J., van, Boomsma, D. I., Ligthart, L., Visscher, C.M. & Jongh, A., de (2015). Self-reported gagging in dentistry: prevalence, psycho-social correlates and oral health. *Journal of Oral Rehabilitation*, 42: 487-494.

[Chapter 7 in this thesis]

Submitted publications related to this thesis

Houtem, C.M.H.H. van, Wijk, A.J. van, Boomsma, D.I., Ligthart, L., Visscher, C.M., Jongh, A. de. The factor structure of dental fear

[Chapter 3 in this thesis]

Other scientific publications

Vermaire, J.H., Houtem, C.M.H.H. van, Ross, J,N. & Schuller, A.A. (*in press*). The burden of disease of dental anxiety; generic and disease-specific quality of life in patients with and without extreme levels of dental anxiety. *European Journal of Oral Sciences.* DOI: 10.1111/eos.12290.

Visscher, C.M., Ligthart, L., Schuller, A.A., Lobbezoo, F, De Jongh, A., van Houtem, C.M.H.H. & Boomsma, D.I. (2015). Comorbid disorders and sociodemographic variables in temporomandibular pain in the general Dutch population. *Journal of Oral & Facial Pain and Headache*, 29: 51-99.

Ligthart, L., Visscher, C.M., Houtem, C. M.H.H. van, Geels, L.M., Vink, J.M., Jongh, A. de & Boomsma, D.I.(2014). Comorbidity Among Multiple Pain Symptoms and Anxious Depression in a Dutch Population Sample. *The Journal of Pain*, 15: 1526-5900.

Ketting, M., Houtem, C.M.H.H. van & Jongh, A., de (2014). De tandheelkundige behandeling bij een patiënt met psychogene pseudo-epileptische aanvallen. *Nederlands Tijdschrift voor Tandheelkunde*, 121: 321-325.

De Jongh, A., Houtem, C.M.H.H. van, Van Der Schoof, M., Resida, G. & Broers, D. (2008). Oral health status, treatment needs, and obstacles to dental care among noninstitutionalized children with severe mental disabilities in The Netherlands. *Special Care in Dentistry*, 28: 111–115.

Houtem, C.M.H.H. van, De Jongh, A., Broers, D.L.M., Schoof, M., van der & Resida G.H.B. (2007). Problemen in de mondzorg voor kinderen met een ernstige verstandelijke beperking. *Nederlands Tijdschrift voor Tandheelkunde*, 114: 129-133.

CURRICULUM VITAE

Caroline Maria Hubertina Henriette van Houtem is op 28 maart 1982 geboren in Sittard. Na haar Gymnasiumdiploma te hebben behaald aan de Trevianum Scholengroep te Sittard is ze in 2000 Tandheelkunde gaan studeren aan het Academisch Centrum Tandheelkunde Amsterdam (ACTA). In 2006 is ze afgestudeerd als tandarts. Na haar afstuderen heeft ze eerst in diverse algemene tandartspraktijken gewerkt en in 2008 is ze als tandarts-angstbegeleiding in opleiding gaan werken bij de afdeling Bijzondere Tandheelkunde van de Noordwest Ziekenhuisgroep locatie Alkmaar. Ook is ze in 2008 begonnen met de post-initiële differentiatie-opleiding tot Tandarts-Angstbegeleiding. Deze opleiding heeft ze in 2012 afgerond.

Haar interesse in het doen van wetenschappelijk onderzoek, in het bijzonder bij bijzondere zorggroepen, is gewekt toen ze twee jaar lang als student-assistent heeft gewerkt bij de vakgroep Sociale Tandheelkunde & Voorlichtingskunde van het ACTA. In 2009 is ze begonnen als parttime Assistent in Opleiding (AIO), wederom bij de vakgroep Sociale Tandheelkunde & Voorlichtingskunde van ACTA. Tegenwoordig werkt ze als tandarts-angstbegeleiding bij de afdeling Bijzondere Tandheelkunde van de Noordwest Ziekenhuisgroep locatie Alkmaar en daarnaast als tandarts-onderzoeker bij TNO Child Health-Mondzorg te Leiden.

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Joske den Engelsen, lieve Joske. 2001: poloshirtje, rode *SCHUIM!*-trui, iets bollere wangen, studeren en af en toe een eindje zeilen. Wat is er sindsdien een hoop in onze levens gebeurd en veranderd. Toch past onze vriendschap zich telkens weer naadloos aan de nieuwe omstandigheden aan. Als geen ander kun jij mij een spiegel voorhouden en me laten inzien wat ik moet doen of juist moet laten. Dank je daarvoor! Sinds 2001 ben je er voor mij op alle belangrijke momenten in mijn leven en daarom ben ik dolblij dat je als paranimf tijdens de verdediging van mijn proefschrift naast me wilt staan.

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