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

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# 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 ( $\pm$ SEM) among specific phobias was for the blood–injury–injection phobia ( $33\% \pm 0.06$ ) and among the fear subtypes this was found for animal fear ( $45\% \pm 0.004$ ). 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 & Hjelmberg, 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 Heuvel 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 Heuvel 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 & Hjelmberg, 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.

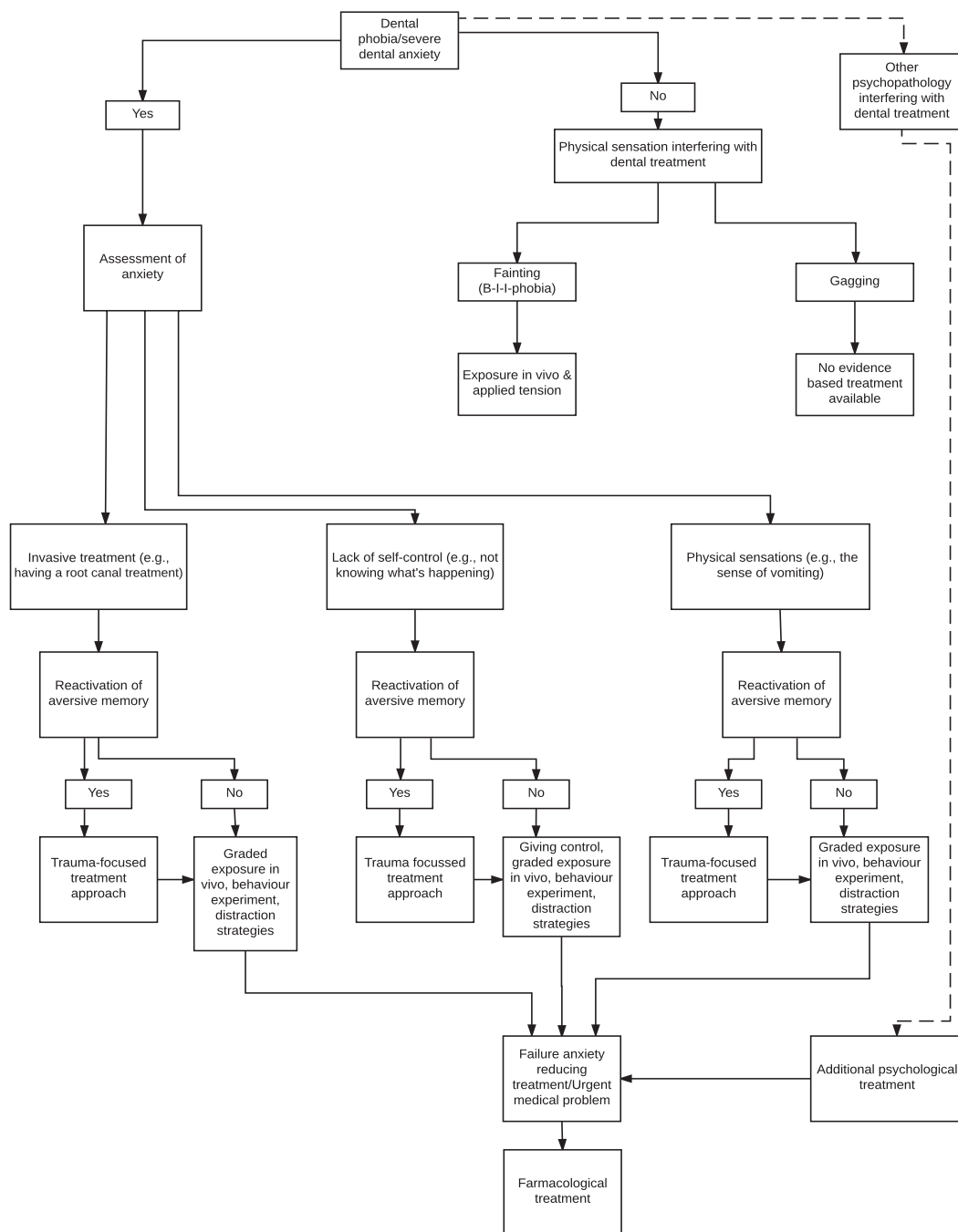
For the oral health professional it is important to note that at this moment, although it may be a disappointing message, the etiology of gagging is far from understood, no evidence based treatment to “cure” all different types of dental gagging is available, and the effectiveness of interventions aiming 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



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