# Cognitive und affective representation of respiratory sensations in health and respiratory disease

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I dedicate this work to my husband Christoph.

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# SUMMARY

*Background*

Dyspnea is a multidimensional construct with qualitatively distinct types of breathlessness that can be distinguished by healthy and diseased individuals. The report of unique sets of these qualitatively distinct respiratory sensations has been shown to be characteristic for specific pathophysiological conditions in a variety of somatic and psychological disorders (Manning & Schwartzstein, 1995; Scano, Stendardi, & Grazzini, 2005). Qualities of physiological sensations cannot be measured other than by self-report of the person who experiences them (e.g. Davenport, 2002). Therefore, the cognitive representation of respiratory sensations has been investigated intensively in recent research. However, sensation report has mostly been analyzed on the level of single sensation descriptors and a direct comparison of the structure of sensation report between healthy and diseased individuals is missing. Furthermore, while discomfort associated with the experience of dyspnea in general has been investigated intensively in recent research (e.g. von Leupoldt, Ambruzsova, Nordmeyer, Jeske, & Dahme, 2006; Wilson & Jones, 1991), little is known about the affective evaluation of specific sensations and dimensions underlying dyspnea-report and on the question how separate sensory and affective dimensions of dyspnea are.

*Aims*

In this doctoral project, we compared the structure of dyspnea report between individuals with different experiential background regarding breathing and breathlessness, such as healthy and diseased individuals, and younger and older individuals. We explored the structure of self-report by integrating clusters of respiratory sensations within a framework of latent dimensions of dyspnea. Besides the cognitive structure of the language of dyspnea, we explored the affective evaluation of clusters and latent dimensions of dyspnea-report in health and disease. We hypothesize that in the cognitive representation of dyspnea, groups of respiratory sensation descriptors can be found that correspond with the activation of different breathing pattern induced by different experimental breathing challenges. Furthermore, we expect that individuals with different experiential backgrounds regarding dyspnea vary in their cognitive representation and affective evaluation of specific respiratory sensations, reflecting different mechanisms of dyspnea in health and disease. Moreover, we hypothesize that affective and sensory components of breathlessness are not separate, but that each sensory experience can be located on an affective dimension between pleasant and unpleasant breathing. Latent sensory dimensions of dyspnea are assumed to contribute simultaneously to the feeling of discomfort associated with breathlessness.

*Methods*

In four studies, we analyzed the report of respiratory sensations after experimental induction of dyspnea as well as in retrospection and compared the cognitive and affective representation of respiratory sensations between younger and older healthy individuals and individuals suffering from respiratory disease. In contrast to prior approaches, we restricted the methods of our analysis not to either cluster analysis or

Multidimensional Scaling (MDS) (Everitt, 1974; Kruskal & Wish, 1994), but combined MDS, cluster analysis, and Preference Mapping (Chang & Caroll, 1998) to explore the language of dyspnea. Also in contrast to most prior research, we did not use an ipsative, but a normative approach which enabled us to compare ratings between groups and to explore the relationship of respiratory sensation report and reported discomfort.

*Results*

The report of respiratory sensations was corresponding with breathing pattern induced by respiratory challenges. Groups of respiratory sensations found with cluster analysis were reflecting different qualities of dyspnea and not different intensity levels of breathlessness. Our results suggest that the complexity of sensation report has been underestimated in prior research. Fewer, but more complex types of dyspnea might be more appropriate to describe the structure of dyspnea. The cognitive representation and affective evaluation of respiratory sensations varied between groups of individuals reflecting different mechanisms and consequences of dyspnea in health, aging and disease. Not all respiratory sensations commonly subsumed under dyspnea are necessarily perceived as uncomfortable by healthy individuals. We found stability of subordinated clusters of respiratory sensations to be limited. Dimensions of dyspnea found with MDS provide a more reliable picture of the structure of dyspnea report than cluster solutions across populations and studies. We found a three dimensional structure with 1) fit between need for air and actual breathing, 2) effort, and 3) attempt of voluntary control as underlying dimensions of dyspnea report. Results found with Preference Mapping suggest that in individuals with and without reported respiratory disease the dimensions fit and effort contribute equally to the experience of discomfort. In older individuals, we found an age related decrease in the differentiation between qualities of dyspnea.

*Conclusion*

While it has been emphasized a number of times how important it is to listen to what patients say about their disease (Davenport, 2002; Mahler & Harver, 2000), this listening might be especially challenging in the language of dyspnea. The interpretation and evaluation of language descriptors of respiratory sensations is highly dependent on the experiential background of the person reporting dyspnea and the context in which these sensations are elicited. Methods to induce dyspnea in experimental research should be chosen carefully regarding the level of compensability of breathlessness for healthy and diseased individuals. Sensation report should not be compared between these groups unless ambiguities regarding the pathological character of a sensation are clarified. Latent dimensions of dyspnea have been found to be less affected by variations in interpretation and evaluation of language descriptors and could help to assess comparability of sensation report between groups with different experiential background regarding breathlessness.

# INTRODUCTION

*Respiratory Sensations: Phenomenon and Underlying Mechanisms*

Dyspnea is defined as "a subjective experience of breathing discomfort that consists of qualitatively distinct breathing sensations that vary in intensity" (American Thoracic Society, 1999, p. 322). It is the agonizing and threatening core symptom in a number of somatic diseases such as respiratory, cardiovascular, and neuromuscular diseases, or cancer (for reviews see e.g. De Peuter et al., 2004; Manning & Schwartzstein 1995; 2001) and psychological disorders (Meuret et al., 2005; Perna et al., 2004), but can also arise in healthy individuals in response to a number of benign stimuli, such as sport and exercise, breathing exercises in yoga and meditation (Brown & Gerbarg, 2005), or strong emotions (Klein, 1993; Roth, 2005; Wientjes & Grossman 1994; Ritz, 2004; Ritz & Steptoe, 2000), as well as during pregnancy (Becklake & Kauffmann, 1999). Eight (Harver et al., 2000; Simon et al., 1989) up to twelve (Eliott et al., 1991) types of dyspnea are discussed in recent research. These types of breathlessness can be distinguished by patients as well as healthy individuals (e.g. Harver, Mahler, Schwartzstein, & Baird, 2000; Simon et al., 1989; 1990).

Research in respiratory medicine has shown that the report of specific types of respiratory sensations is related to different physiological mechanisms. There is no single dyspnea receptor, but ventilation is monitored by multiple sensory systems. The four most important system-categories are 1) muscle afferents (mainly intercostal muscles and diaphragm), 2) stretch receptors in the lungs, 3) irritant receptors in the airways, and 4) chemoreceptors in the brain stem (Manning & Schwartzstein, 1995; O'Donnell et al., 2007). Respiratory sensations are produced by changes in the activation of one or more of these groups of afferents. Stimulation of irritant receptors within the airways plays a role in the perception of obstruction as well as stimulation of sensory receptors within the lungs mediated through vagal and other autonomic pathways. Activation of chemoreceptors within the central nervous system that are sensitive to changes in partial pressure of $CO_2$ can elicit the feeling of air hunger, while an increase in motor command to ventilatory muscles can lead to feelings of effort. Furthermore, a mismatch between respiratory motor command from the brain stem and higher brain centres to respiratory muscles on the one hand and the afferent response from the respiratory system on the other hand could result in a more complex pattern of mechanisms and sensations accumulating in the perception of unsatisfactory respiration (Scano et al., 2005). It is assumed that respiratory sensations that can be reliably discriminated are based on different mechanisms, whereas symptoms that cannot be clearly discriminated are based on similar mechanisms (American Thoracic Society, 1999; Manning & Schwartzstein, 1995; Binks, Moosavi, Banzett, & Schwartzstein, 2002; Lansing, Im, Thwing, Legedza, & Banzett, 2000; Moy, Wodrow-Weiss, Sparrow, Israel, & Schwartzstein, 2000).

The perception of respiratory sensations, however, is not a sole result of the activation of afferent systems or processing of afferent-efferent mismatches, but is additionally depending on the cognitive, behavioral and affective state of the person. A respiratory sensory gating system model has been proposed (e.g. Davenport, 2007), which is conceptualized in analogy with the gate theory of pain (Melzack & Wall, 1965; Wall & Melzack, 1962). The first level in this model is the attentional modulation of gating. To perceive a respiratory sensation we have to change our cognitive state and attend to our ventilation. Until this change in attention, the mechano-sensory information about respiration is gated out of the cognitive centers. Such a change in awareness of breathing requires a sufficiently strong change in information coming from the respiratory system. The magnitude of this threshold depends on the background status of the respiratory system as well as on external or internal cues that are not related to respiration, but might lead attention away from respiration (e.g. Thornby, Haas, & Axen, 1995), learning processes (e.g. De Peuter et al., 2005; Killian, 1985), and affective states (e.g. Put, Demendts, Van den Bergh, Demyttenaere, & Verleden, 1999;

Van den Bergh et al., 2004). Thus, in the perception of respiratory sensations, afferent information is received by the respiratory center in the brain stem and filtered by a neural integrator or gate. In this filtering process, the ‘association cortex’, plays a major role, i.e. the brain regions that are mediating attention, thoughts, and experience, as well as the limbic system, mediating emotional states (Davenport, 2007, p. 148). If the signal strength from the respiratory system is larger than the state dependent threshold, some of this information is processed in the somatosensory cortex, leading to conscious detection. In a second stage of this model of respiratory perception, affective awareness and evaluation takes place, i.e. the decision whether breathing has a comfortable or uncomfortable quality. This affective evaluation is crucial for voluntary as well as involuntary attempts for compensation and control of dyspnea (Banzett, Dempsey, O’Donnell, & Wamboldt; 2000; Davenport, 2007).

Because experience and learning play a role in the perception of respiratory sensations, it can be assumed that variables such as age, gender, and culture influence perception and report of dyspnea (for reviews see De Peuter et al., 2004; Rietveld & Brosschot, 1999). However, empirical support for this assumption is inconsistent. While some studies found an association of age with accuracy of symptom perception (e.g. Tetzlaff, Leplow, ten Thoren, & Dahme, 1999), others found no age effect (e.g. Ottabelli et al., 2000). Also, in studies exploring the effect of gender, inconsistent results are found (for a review see De Peuter et al., 2004). Moreover, studies have shown that the perception of bronchoconstriction in asthma patients fluctuates during the day, with less accuracy in the afternoon than in the early morning (Rietveld & Prins, 1998). Instead of a stable influence of demographic and health related variables on the perception and report of all types of respiratory sensations, it could be assumed that the influence of expectations and learned schemata on the perception of respiratory sensations is more pronounced when a sensation is ambiguous. It has been shown that the more ambiguous physiological sensations are, the more context factors will become important for evaluation and interpretation such as the behavior of relevant others (Schachter & Singer, 1962), or situational cues (Berkowitz, 1993). In asthma, breathing-related and breathing-unrelated variables such as false breathing sounds (Rietveld, Kolk, Prins, & Colland, 1997) or social pressure (Rietveld, Van Beest, & Everaerd, 1999) have been shown to influence breathlessness ratings. Physiological differences between groups, as well as differences in believes about causes and consequences of dyspnea that vary in relationship with age, gender, culture, and health status might be most pronounced in the report of dyspnea when respiratory sensations are mild and cannot clearly be related to pathophysiological processes or to external variables such as exercise. In line with this assumption, the association of negative affect with perception and report of general feelings of dyspnea has been shown to be most pronounced, when symptoms are mild and ambiguous (Chen, Hermann, Rodgers, Oliver-Welker, & Strunk, 2006).

*The Relevance of the Affective Evaluation of Sensations in Dyspnea*

The affective evaluation of dyspnea is of importance because it is the very component of dyspnea that evokes distress and motivates behaviors such as avoidance of stimuli or seeking help (Banzett et al., 2000). General intensity and discomfort of dyspnea have been explored in studies using the Borg scale with healthy controls (e.g. von Leupoldt et al., 2006; von Leupoldt & Dahme, 2005; Wilson & Jones 1991) or visual analogue scales in patients with COPD (Carrieri-Kohlman, Gormley, Douglas, Paul, Stulbarg, 1996). Von Leupoldt et al. (2006) have shown that sensory and affective aspects of dyspnea contribute differentially to the report of experience of general feelings of dyspnea. However, the affective connotation of single respiratory sensations has not been explored so far. The practice of measuring the affective evaluation of dyspnea by including descriptors of emotional states in dyspnea questionnaires, as done in prior research (e.g. Kinsman, Luparello, O'Banion, & Spector, 1973; Skevington, Pilaar, Routh, & Macleod, 1997), may not be appropriate. In asthma, questionnaires separating respiratory symptoms from their affective evaluation have not yielded largely divergent findings for these two components of dyspnea (e.g. Steen et al., 1994). Instead of a separate affective dimension of dyspnea, each sensory respiratory sensation can be assumed to have its own affective connotation. Some authors have recently drawn a parallel between dyspnea and pain sensations (Banzett & Moosavi, 2001). For pain, Clark et al. (2001) have demonstrated that although semantically sensory, emotional and motivational dimensions can be distinguished, these dimensions are highly interrelated and the sensory dimension of pain is not independent from evaluation. Clark et al. (2001) concluded that "a score on a pain rating scale is not a pure measurement of the patients pain, but is heavily influenced in unknown ways by the patient's emotional and motivational state" (p. 38). The same could be expected in dyspnea, but the distinctiveness of sensory and affective components of different respiratory sensations has not been explored so far.

Given the dependency of sensations on emotion and motivation, it would be fair to speculate that the affective evaluation of sensory respiratory sensations would vary between individuals with different experiential background regarding dyspnea, such as patient groups and healthy individuals, analogous to variations of causes and consequences of breathlessness between these groups. For instance, prior research has shown that effort is associated with high discomfort in asthma patients, but is not perceived as uncomfortable by healthy individuals as long as blood gas levels remain normal (Banzett et al., 2000). While both groups might choose the same descriptors to describe their respiratory sensations, the affective connotation of these sensations might be very different. Comparing self-report between these groups can lead to invalid conclusions, as long as potential differences in the affective evaluation of words used to describe sensations are ignored. More knowledge of the affective evaluation of specific respiratory sensations in healthy individuals and patient groups would be important to clarify benefits and limits of using healthy samples as comparison groups in clinical dyspnea research.

Furthermore, focusing more on the affective component of dyspnea could be especially important in exploring poor symptom perception and inadequate disease management in patient groups. It could be argued that no diagnosis is complete without a thorough physiological examination, and that methods such as e.g. tests for airway hyperreactivity in asthma are more important for a diagnosis than the report of the subjective impression a patient has of the state of his or her airways. For the successful self-management of a disease however, accuracy of symptom perception is regarded to be fundamental. Detection of asthma symptoms has been reported to be inadequate in 15% (Banzett et al., 2000; Rubinfeld & Pain, 1976) up to 60% of patients (Kendrick, Higgs, Whitefield, & Lazlo, 1995). Some patients fail to report serious increase in airway obstruction, while others report severe symptoms without any physiological changes. While the first is leading to delay in seeking help, to inadequate utilization of medications, and to near fatal or fatal asthma attacks (Banzett et al., 2000; Kikuchi et al., 1994), the latter may lead to overuse of medical service and to overuse of medication with potentially dangerous side effects, such as the over-use of ß-agonists that has been linked to an increased mortality (e.g. Cockcroft, 2006). It remains unclear, whether patients showing inaccurate symptom report have problems actually perceiving symptoms or if such an inaccurate report reflects an interpretational bias (De Peuter et al., 2004). It could be expected that individual differences in symptom perception and disease management are partly related to differences in the affective evaluation of specific sensations in terms of perceived distress associated with them. In line with that, De Peuter et al. (2008) have shown that catastrophic thinking about asthma is associated with over-report of symptoms. Studies have also shown that affective associations, i.e. feelings related to a disease, mediate the relationship of illness-related cognitions and illness related behavior such as disease management (Kiviniemi, Voss-Humke, & Seifert, 2007). The hot/cool model of cognitions (Metcalfe & Mischel, 1999, see also Damasio, 1999) suggests that cues designed to activate 'hot', emotional systems will typically dominate attention and promote relevant behavior more than cues designed to activate 'cool' cognitive systems. Following the assumptions of this model, it could be hypothesized that the affective evaluation of respiratory sensations will be related to attention towards disease related cues and its interpretation and report, even though such an affective evaluation is not as strongly negative as catastrophic thoughts. Furthermore, affective evaluation of symptoms being rather moderate to low in negativity could be assumed to be related to an underestimation of danger associated with these symptoms, delay in seeking help, and underreport of sensations. This assumption has received empirical support in the field of research on pain. It has been shown that a stoic, i.e. non-emotional attitude towards pain in older individuals can lead to an under-report of pain (Yong, Gibson, & Horne, 2001). Therefore, including affective evaluation in the analysis of the report of respiratory sensations could help to evaluate comparability of sensation-report between groups and to gain a deeper understanding of the relationship between sensation report and health-behavior.

*Quantifying and Analyzing the Perception of Respiratory Sensations*

The experiential aspect of dyspnea can only be quantified by the person who is experiencing it, either by verbal self report or in a nonverbal mode, such as e.g. using a hand dynamometer, where grip strength serves as a measure of perceived respiratory symptoms (Tetzlaff et al., 1999). Self-report data traditionally has been viewed with considerable scepticism (Smith, Wallston, & Dwyer, 1995). Stevens (1971) and others (for a review see e.g. Marks, 1974; Killian, 1985) however, have shown that individuals can quantify the magnitude of a sensory experience in a reliable and meaningful sense. For equal physical ratios, there are equal sensory ratios which are constant. Intensity of dyspnea and feelings of discomfort accompanying this sensation are usually measured with i) ordinal word scales, ii) the Borg Scale combining verbal categories such as “very slight” or “severe” with numerical values (Borg, 1982), iii) visual analogue scales where no verbal or numerical categories are presented, but the subject is free to select any point on such a scale, or iv) word labeled visual analogue scales (Lansing, Moosavi, & Banzett, 2003). It has been found that intensity of general feelings of dyspnea rated on such scales by individuals suffering from asthma during exercise is reliable related to physiological parameters, such as peak inspiratory flow, tidal volume, respiratory rate, and peak inspiratory mouth pressure (Mahler et al., 1991). These scales can be used to quantify general feelings of dyspnea, but also to assess intensity of discomfort associated with specific qualities of breathlessness. However, because dyspnea is a multidimensional construct and respiratory sensations that can be discriminated may imply different physiological mechanisms of dyspnea (American Thoracic Society, 1999), knowledge about the structure of the cognitive representation of dyspnea in terms of distinct categories of respiratory sensations and of underlying dimensions can be crucial in improving the diagnostic value of self-report of respiratory sensations.

A number of methods and approaches are available to explore self-report that cannot be regarded to be interchangeable. Researchers have the choice between psychometric versus psychophysiological approaches addressing either the situational or general structure of dyspnea. Furthermore, either dimensions, or categories of dyspnea, or both can be explored and the data on which such analyses are based can be gathered in a normative or in a forced choice approach. Every choice in methods and approaches has important implications for research questions that can be addressed and the interpretation of results. In the following paragraph, we review the conceptual and methodological background of the analysis of self-report of physiological sensations and outline advantages of combining categorical and dimensional approaches.

*Psychometric versus psychophysiological approaches in analyzing multidimensional constructs*

The language of dyspnea has been explored with methods such as cluster analysis (e.g. Elliott et al. 1991; Mahler et al. 1996; Simon et al., 1989;1990; von Leupoldt et al., 2007), multidimensional scaling (MDS) (Harver et al., 2000; Skevington et al., 1997), or factor analysis (Perna et al., 2004). These multivariate methods share a number of similarities. However, because these methods have been developed in different traditions with different underlying assumptions and aims, each method is providing different insight into the cognitive representation of dyspnea. Table 1 presents a selection of the most important differences between factor analysis on the one hand and MDS and cluster analysis on the other.

Table 1: Brief overview of differences between factor analysis and MDS and cluster analysis

| | Factor analysis | MDS and cluster analysis |
|---|---|---|
| Tradition | Psychometrics<br><br>Psychology of personality and intelligence | Psychophysics<br><br>Thurstone's law of comparative judgments (Thurstone, 1927) |
| Basic measure | Correlations (positive or negative) between objects | Either mutual similarities or distances (both can be positive only) between objects or concepts |
| Data structure | Values of *m* variables assessed in *n* individuals with regard to one concept (agreement, intensity, etc.) | $k$ $(k\text{-}1)/\ 2$ mutual comparisons of $k$ objects by $n \geq 1$ individual(s) with regard to several attributes simultaneously |
| Selection of variables | Variables have to be selected by the researcher | Attribute free approach is possible, as well as selection of attributes by the researcher |
| Aim | Categorizing data and eliminating specific variance of single variables<br><br>Finding underlying factors behind linear relationships | Cluster analysis: Finding clusters that are as homogeneous and as different from other clusters as possible<br><br>MDS: Finding underlying dimensions or meaningful partitions of a *m*-dimensional space; dimensions can, but do not have to be linear (e.g. circular dimensions of a color space) |
| Knowledge gain | Creating hypothesis about factors underlying interrelations of variables | Theory development and optimizing models of perception |

Factor analysis was originally developed in the field of psychometrics to explore factors underlying intelligence (for a historical overview see e.g. Bartholomew, 1995). It aims to categorize variables and to explore latent variables underlying positive and negative interrelations in a data set. Factor analysis was developed to analyze traits such as intelligence that are assumed to be stable across time and situations. It can be regarded to be less adequate for the analysis of more complex constructs that are varying in structure depending on the context such as dyspnea. Most factor analysis techniques can not explore a comprehensive structure of dyspnea, but only the structure of dyspnea specified within a situation, such as breathlessness experienced in individuals suffering from panic disorder during a panic attack (Perna et al., 2004) (for an exception see the p-technique, Cattell, 1951). In contrast, MDS and cluster analysis have been developed as theories of perception rather than statistical methods (Torgerson, 1958). They are rooted in the tradition of psychophysiological research on the perception of context-dependent states and offer the advantage of exploring dimensions and types of dyspnea by including *multiple* aspects of dyspnea *simultaneously*, such as e.g. to explore dyspnea experienced in response to different stimuli or in different situations simultaneously in one analysis. Using these methods, similarity of item-profiles across situations or experimental conditions either for one individual or a group of individuals is the source of information, not positive or negative correlations found in a group of individuals reporting qualities of dyspnea in a single experimental condition. The perception of dyspnea is based on complex processes and can arise in response to a multitude of different mechanisms as it has been described above. While it is assumed that groups of *similar* respiratory sensations are related to similar physiological processes, sensations that are positively and negatively *interrelated* could be assumed to be related to different physiological mechanisms, but load high on the same factor. Therefore, MDS and cluster analysis can be regarded as preferred methods for analyzing perception and report of respiratory sensations and have been favored in most studies on the language of dyspnea (e.g. Elliott et al. 1991; Mahler et al., 1996; Simon et al., 1989; 1990; von Leupoldt et al., 2007; Harver et al., 2000; Skevington et al., 1997) to gain insight in the general structure of perception and report of respiratory sensations.

*Categories vs. dimensions of dyspnea*

Categories of perceptual qualities of dyspnea have been found to correspond to an activation of one or more of the four major categories of afferents in the respiratory system (Manning & Schwartzstein, 1995; O'Donnell et al., 2007). Therefore, it could be concluded that a categorical approach using cluster analysis is the most adequate way in analyzing the structure of sensation report mapping types of dyspnea with types of physiological mechanisms. However, the question whether to describe a construct in terms of categories or dimensions cannot be an either/or question (Meehl, 1999). In cognitive linguistics, category membership is regarded to be gradual with no clear cutoff (e.g. Rothbart & Taylor, 1992; see also Rosch 1975; 1978; Smith & Medin, 1981). Diagnosis in medicine and psychology is still very much influenced by the classical Aristotelian view that is based on categories (e.g. Acton & Zodda, 2005; Carson, 1996). However, recently a conceptual and methodological approach to the dimension/category controversy has been developed, the dimension/category framework that integrates categorical and dimensional approaches (De Boeck, Wilson, & Acton, 2005). According to this approach, manifest categories and their indicators (e.g. symptoms) can be explained in terms of latent categories such as questionnaire items and latent dimensions. The dimension/category framework was developed as a new approach to the classification of psychopathology built on a dimensional foundation. However, this approach could also be fruitful for an understanding of the report of physical sensations. We oriented our analysis of the report of respiratory sensations along this theoretical framework and explored, whether descriptors of respiratory sensations can be regarded as latent categories of manifest categories of breathing patterns, i.e. we explored, whether report of respiratory sensations is reflecting breathing pattern induced by experimental respiratory challenges. In a second step, we explored whether these latent categories of dyspnea can be explained by latent dimensions of dyspnea. For this purpose, we embedded clusters found in the analysis of respiratory sensation report within latent dimensions found with MDS and explored whether these dimensions can provide further information about factors underlying the formation of clusters and provide additional information about the cognitive structure of dyspnea.

*Structure and complexity of the report of respiratory sensations*

In prior studies comparing the report of respiratory sensations between groups, such as patients with cardio-respiratory disease and healthy individuals, cluster structures of sensation descriptors were derived across all participants combining ratings of healthy controls and ratings of different patient-groups. Groups were compared only with regard to this general structure (Eliott et al., 1991; Mahler et al., 1996; Simon et al., 1990; Skevington et al., 1997). Possible differences in the structure of self-report between groups with different experiential background regarding dyspnea have received little attention so far, although it can be expected that the structure of the language of dyspnea differs between groups at least on higher levels of aggregation, with different pathophysiological condition being characterized by unique sets of sensations (Manning & Schwartzstein, 1995; Scano et al., 2005).

Furthermore, the question of the appropriate number of sensation clusters to be interpreted as distinct types of dyspnea has received only little attention so far, although this decision is crucial in understanding sensation report. Only categories of sensation that are sufficiently homogeneous as well as sufficiently distinct from each other could be related to distinct physiological mechanisms (Manning & Schwartzstein, 1995; Scano et al., 2005). However, mostly cluster structures on a low fusion level were in the focus of interest in recent research, with 8-12 smaller clusters of low complexity (e.g. Elliott et al., 1991; Harver et al., 2000; Mahler et al., 1996; Simon et al. 1989; 1990). The decision of the number of clusters was mostly done by visual inspection of a hierarchical dendrogram, not taking into account that clusters reflect only relative degrees of similarity between concepts. Hierarchical cluster analysis however, will always lead to the formation of categories in every group of concepts no matter how similar or dissimilar these concepts are, unless all concepts are constant in all attributes (Everitt, 1974). A number of methods have been suggested to determine the appropriate number of clusters, such as the inspection of a scree plot displaying a heterogeneity coefficient as a function of the numbers of clusters. Only when the decrease in heterogeneity is strong enough, a higher number of clusters should be considered. Furthermore, discriminant analysis using clusters as grouping variables can help decide whether clusters are not only sufficiently homogeneous, but also sufficiently separated from each other to be considered as distinct constructs. In addition to these methods, Everitt (1974) as well as Kruskal and Wish (1994) have suggested to combine the analysis of categories with the analysis of latent dimensions underlying the formation of clusters. In doing so, objects or concepts can be described as n-dimensional coordinates in an n-dimensional space. Clusters can be defined as continuous regions in this space with a relative high density of points separated from other such regions by areas with a relative low density of points. Clusters described in this way are sometimes referred to as *natural clusters* (Everitt, 1994, p. 44). The optimal number of distinct types of dyspnea in terms of such natural clusters has not been assessed so far. Studies have reported cluster solutions consisting of 8 up to 10 subclusters of respiratory sensations (e.g. Harver et al., 2000; Simon et al., 1990). Respiratory medicine however, suggests only four major afferent systems to be related to the experience of dyspnea (Scano et al., 2005). Thus, it could be expected that a smaller number of such natural categories of respiratory sensations (in terms of descriptor groups reflecting distinct physiological mechanisms) can be found than is suggested by recent research on the language of dyspnea. Therefore, exploring the structure of dyspnea combining cluster analysis with MDS is appropriate from both a theoretically point of view (as suggested by the dimensional/ categorical framework, De Boeck et al., 2005) as well as a methodological perspective.

A study of Harver et al. (2000), exploring the report of dyspnea in healthy individuals, can serve as an example of the benefit of combining cluster analysis and MDS in the analysis of respiratory sensations in a joint presentation. Figure 1 shows the dendrogram identified in this study using hierarchical cluster analysis and the Average-Linkage algorithm. Figure 2 shows the MDS configuration that was found on basis of the same data as the cluster structure in this study using ordinal MDS. These two results found with cluster analysis and MDS in one data set were reported, but *not* combined in a joint presentation by Harver et al. (2000). Figure 3 shows how the clusters identified by Harver et al. (2000) can be embedded as ellipses within the MDS space. To create this figure, we used the MDS configuration generated by Harver et al. (2000) and drew ellipses representing the eight clusters using a standard computer program for text editing (Word, Microsoft). The smaller clusters in the right half of the configuration show overlaps when the eight clusters are embedded. Embedding ten clusters would have been possible without overlaps, however, in doing so seven outliers would have been identified in a group of 15 items that would have been less distinct from each other than the three items of the cluster subsuming rapid, more, and heavy breathing.

On the basis of a joint presentation of the data reported in this study by Harver et al. (2000), it could be argued that healthy individuals organize their cognitive representation of respiratory sensations along two superordinated clusters that could be interpreted as 1) *compensation of dyspnea*, subsuming sensations being rather benign for healthy individuals such as rapid breathing and breathing more on the one hand and 2) *breathing deficiencies* on the other hand, such as suffocating and air hunger, located in the half of the MDS configuration interpreted as "Hindered or obstructed breathing" by Harver and colleagues (2000). In Figure 3, this superordinated cluster is displayed by us using a dotted line. The overlap between two of the smaller cluster suggests, that a solution with two superordinated clusters instead of 8 clusters would be more appropriate for these data.

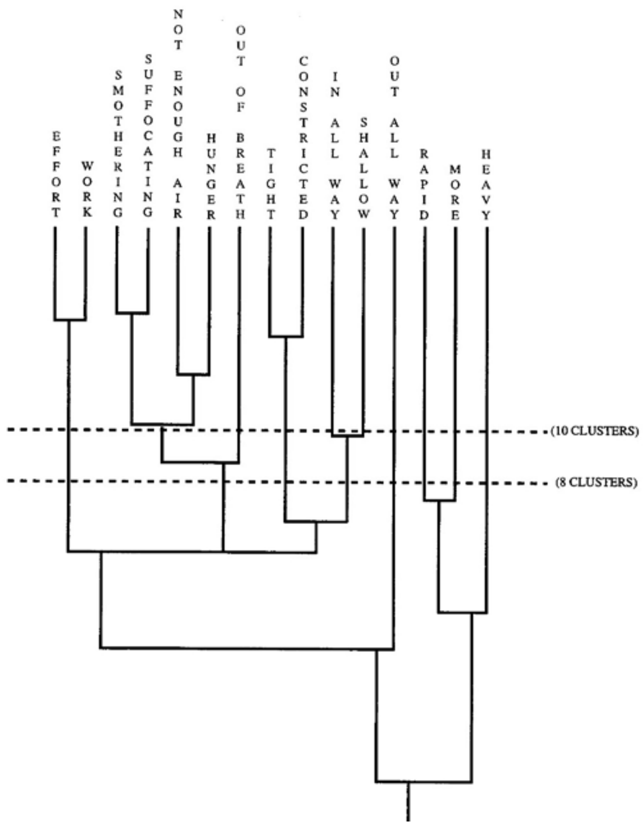


Figure 1: Hierarchical cluster structure of respiratory sensations, identified by Harver et al. (2000) (From: Harver, A., Mahler, D.A., Schwartzstein, R.M., & Baird, J.C. (2000). Descriptors of breathlessness in healthy individuals. Distinct and separable constructs. *Chest, 118,* p. 684, Copyright © 2000 by American College of Chest Physicians).

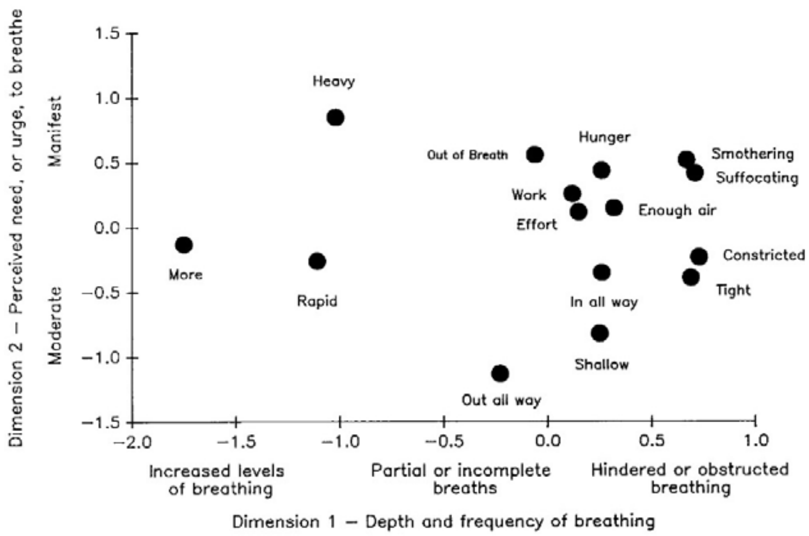


Figure 2: MDS configuration of respiratory sensations identified by Harver et al. (2000) (From: Harver, A., Mahler, D.A., Schwartzstein, R.M., & Baird, J.C. (2000). Descriptors of breathlessness in healthy individuals. Distinct and separable constructs. *Chest, 118,* p. 686, Copyright © 2000 by American College of Chest Physicians).

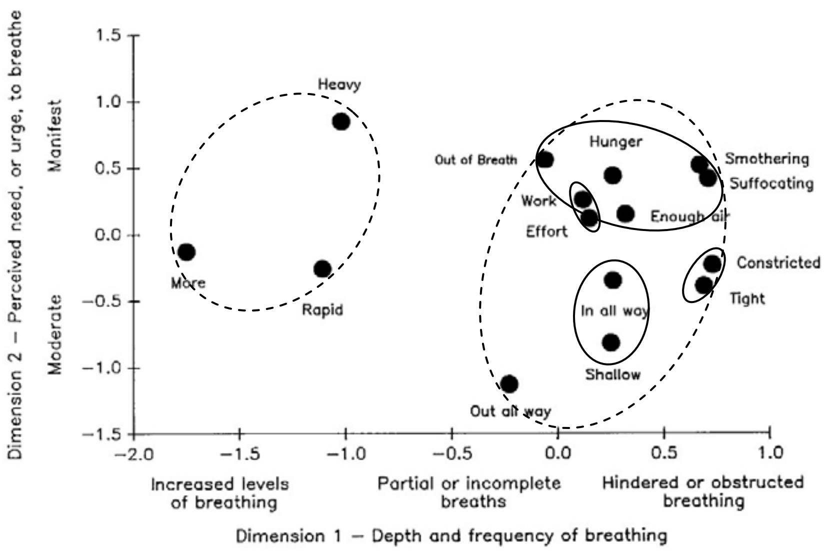


Figure 3: Joint representation of clusters embedded by the author of this report as ellipses within the MDS configuration of respiratory sensations identified by Harver et al. (2000). Ellipses drawn by using a dotted line represent the superordinated clusters interpreted as 'compensation of breathing' (left side of the configuration) and 'breathing deficiencies' (right side of the configuration) suggested by the author of this report (Adapted from: Harver, A., Mahler, D.A., Schwartzstein, R.M., & Baird, J.C. (2000). Descriptors of breathlessness in healthy individuals. Distinct and separable constructs. *Chest, 118,* p. 682, Copyright © 2000 by American College of Chest Physicians).

*Forced choice versus ipsative approaches in measuring qualities of dyspnea*

The majority of studies on the report of respiratory sensations has assessed experiential qualities of dyspnea by asking participants to choose among a list of descriptors of respiratory sensations and to select one to three items that would describe their feelings of breathlessness most accurately (e.g. Moy, Latine, Harver, & Schwartzstein, 1989; Binks, Moosavi, Banzett, & Schwartzstein, 2002; Coli et al., 2006; Morélot-Pazini et al., 2006; Perna et al., 2004). This method is known as forced-choice approach and is yields only ipsative measures. Another possibility to assess qualities of dyspnea would be a normative approach investigating Likert-type ratings for a whole list of descriptors of respiratory sensations. Likert-type scale have several advantages over the forced choice method. Scores from Likert-type scales can be compared across groups of individuals, scores from ipsative measures cannot (Baron, 1996). Furthermore, the forced choice approach increases the probability of random answers and produces less reliable results than normative measures (Blinkhorn, Johnson, & Wood, 1988). While a forced choice assessment offers advantages in a medical setting, where it helps to gain immediate information on the individual state of a patient in an emergency situation, it might be less useful in a controlled experimental setting. Furthermore, in analyzing scores from ipsative measures statistical standard procedures are not available to explore the association of dyspnea intensity ratings with other variables, such as perceived discomfort.

*The Aim of this Doctoral Project*

Information on the quality of a physiological experience can only be provided by the individual perceiving it. Even though self-report data traditionally has been viewed with considerable scepticism (Smith et al., 1995), we argue that it cannot be assumed that self-report is inherently unreliable. Smith et al. (1995) have suggested that in “examining rather than discounting” (p. 72), it should be possible not only to interpret self-report with greater precision, but also to generate valuable insights into the processes associated with coping with symptoms and adaptation to physiological processes. In exploring self-report of dyspnea, the cognitive structure as well as the affective evaluation of sensations can offer valuable information. This includes also exploring possible misconceptions about causes and consequences of dyspnea and individual differences in the interpretation of language descriptors. Only when the cognitive and affective structure of dyspnea, as well as its relationship to context variables and the interaction with mood states is known, the reliability and validity of self-reported respiratory sensations can be assessed. Language is dynamic and often ambiguous. However, this makes self-report of physiological sensations not less important or less useful for research and clinical practice. Understanding in which situations and in which groups of individuals variations in the cognitive structure and affective evaluation of symptoms can be found will support the understanding of physiological mechanisms, as well as of coping mechanisms and adaptation to symptoms.

Therefore, we compared the structure of dyspnea-report between individuals with different experiential background regarding breathing and breathlessness, such as individuals with and without known respiratory disease and younger and older individuals. We explored the structure of self-report by integrating clusters of respiratory sensations within a framework of latent dimensions of dyspnea. Besides the cognitive structure of the language of dyspnea, we explored the affective evaluation of clusters and latent dimensions of dyspnea-report in health, aging, and disease. Our hypothesis can be summarized in the following four assumptions:

H1: In the cognitive representation of dyspnea, latent categories of respiratory sensation descriptors can be found that correspond with breathing pattern induced in experimental respiratory challenges. These latent categories of dyspnea can be explained by their location on latent dimensions of dyspnea.

For clinical practice and diagnosis, this would mean that self-report can provide useful information about physiological processes. For research this would mean that this information can be analyzed on different hierarchical levels of perceptual organization and that categories themselves can not be regarded to be absolutely distinct, but organized along dimensions in a meaningful way.

H2: Affective and sensory components of breathlessness are not separate, but each sensory experience has a specific affective connotation.

For research on the report of dyspnea, this would mean that using descriptors of affective states to assess the affective evaluation of dyspnea might not be appropriate, but affective evaluation should be assessed separately for each sensation. For clinical practice, this would mean that therapy of respiratory symptoms should not only target the intensity of a sensory experience, but also the affective evaluation of sensory qualities to lead to an overall elevation of the burden of the disease.

H3: Individuals with different experiential backgrounds regarding dyspnea differ in their cognitive representation and affective evaluation of specific groups of respiratory sensations reflecting different mechanisms of dyspnea in health and disease.

For research on the language of dyspnea, this would mean that report of respiratory sensations in different groups of individuals such as patients suffering from cardio-respiratory disease and healthy individuals might not be comparable, even though both groups may use the same words. Variations between groups in the cognitive organization of sensations into categories on higher levels of perceptual organization should be regarded as source of diagnostic information. The same can be assumed for variations between groups in the affective evaluation of sensations.

H4: Different latent sensory dimensions of dyspnea are contributing simultaneously to the feeling of discomfort associated with breathlessness.

For clinical practice, this would mean that attempts to change the evaluation of dyspnea, e.g. in individuals having catastrophizing thoughts about benign respiratory sensations, need to target the whole cognitive-affective framework a patient has about breathlessness and not specific sensations or emotions in isolation.

*Methods Used in this Doctoral Project to analyzed the Cognitive and Affective Representation of Respiratory Sensations*

Cluster analysis, MDS, and Preference Mapping are labels used for families of statistical techniques subsuming a number of different algorithms and approaches to analyze similarities between objects or concepts and the affective evaluation of dimensions underlying similarity judgments. While methodological and theoretical questions regarding the application of these methods have been discussed above, we will describe in the following paragraphs the specific algorithms and indices which we have chosen for our analysis reported in Chapter 1-4. For all analyses, if not indicated otherwise, we used the XLstat program (Addinsoft, New York).

*Approaches to collect similarity ratings as basis for cluster analysis, MDS, and Preference Mapping*

Cluster analysis, MDS, and Preference Mapping are based on the analysis of mutual similarities between items. Similarity ratings can be collected directly for pairs of objects in an attribute free approach (see e.g. Harver et al., 2000). In doing so ($k$ ($k$-1)/ 2) similarity ratings for $k$ pairs of objects are given. However, in using this direct approach it can not be explored whether different clusters and dimensions of a construct such as dyspnea correspond differently to specific attributes of the concept in question, such as e.g. different clusters and dimensions of dyspnea could correspond differently to variations in experimentally induced breathing patterns. The correspondence of clusters of reported respiratory sensations with experimentally induced breathing patterns, respiratory parameters, and everyday situations eliciting dyspnea was of central interest in the studies reported in Chapter 1-4. Thus, we asked participants to report respiratory sensations with regard to their experience in or after experimental induction of different breathing pattern (Chapter 1 and 2) or in retrospection with regard to a number of situations that are likely to produce different pattern of respiratory sensations (Chapter 3 and 4) and did not use an attribute free approach.

*Identifying latent dimensions: distance measures and fit indices in MDS*

In MDS, dimensions underlying the cognitive representation of a construct are identified. Thus, one aim of this method is data reduction. The smaller the number of objects or items and the higher the number of dimensions on which these items are organized, the more trivial such a reduction might be, such as in the hypothetical case of four objects being represented on four dimensions, each high on one dimension and low on the others. Thus, the relation of the number of objects, in our case descriptors of dyspnea to dimensions is important. The heuristic rule of Kruskal and Wish (1994) states that:

$$I\text{-}R > 4\,R$$

where $I$ is the number of objects (descriptors of dyspnea) and $R$ is the number of dimensions of the perceptual space in which objects are displayed. To interpret 3 dimensions, the number of objects should be greater than 13, which is met in our studies reported here (Chapter 1-4), exploring the representation of 15-25 items describing respiratory sensations.

MDS can be computed as metric or ordinal MDS. In ordinal MDS, rank order of distances in the perceptual space should correspond to the order of corresponding similarity ratings. If there are two objects pairs with the same rank regarding similarity, then there are no restrictions on the corresponding distances, i.e. dissimilarities of the same rank need not necessarily give equal distances in the representation space. In metric MDS, similarities are considered as continuous and have to be reproduced as closely as possible in the corresponding distances in the perceptual space. In the studies reported in Chapter 1-4 ordinal MDS was used. Exploratory analysis showed that results obtained with metric MDS did not differ substantially.

To compute mutual distances from similarity ratings for object pairs, different distance indices can be used. We decided to use the two indices most frequently used in MDS and cluster analysis, 1) squared Euclidian distances which can be used for the analysis of metric data (studies reported in Chapter 1 and 2) and 2) $Chi^2$ metric which can be used for the analysis of nominal data (studies reported in Chapter 3 and 4). Both distance measures compute the distance between two points in a perceptual space in terms of their direct, i.e. shortest distance in contrast to e.g. the city block metric (Kruskal & Wish, 1994).

To decide whether mutual distances in the perceptual space are representing mutual dissimilarities in the data in an appropriate way, a so called stress index can be computed (Kruskal, 1964). This index is assessing the lack of fit between distances in a MDS configuration to the corresponding ratings of similarities. Small stress values indicate a good model fit. As a convention, a stress value of .2 is regarded to indicate poor fit, a value of .1 fair fit, .05 good fit, .025 excellent fit, and 0 perfect fit. Stress decreases, when more dimensions are included within the model. Thus, model fit has to be interpreted not as absolute value, but in relation to the number of dimensions in a model.

MDS, cluster analysis, and Preference Mapping could theoretically be applied to analyze similarity ratings given by one person only. When the ratings of more than one person are analyzed, such as in the studies reported in Chapter 1-4, these ratings can be averaged across participants (for the more complex analysis of individual difference scaling in a three way MDS, known as INDSCAL see Caroll & Wish, 1974).

*Identifying clusters: distance indices and algorithms in agglomerative and k-means clustering*

In cluster analysis, mutual distances from similarity ratings for object pairs are computed in the same way as in MDS. As in MDS, we used squared Euclidian distances for the analysis of metric data in studies reported in Chapter 1 and 2 and $Chi^2$ metric for the analysis of nominal data in studies reported in Chapter 3 and 4.

Clusters can be identifies with agglomerative hierarchical approaches or with *k*-means analysis. Agglomerative methods of hierarchical cluster analysis combine items to clusters by starting with small subclusters of highly similar objects that merge with each step to larger groups, building hierarchical structures in a bottom-up process. The algorithm stops when all objects are combined into a single cluster (Everitt, 1974). Different criteria can be used to decide which clusters are similar enough to be merged to a superordinated cluster such as (among others) Single Linkage, Average Linkage or the Ward method. In Single Linkage, subclusters are combined on the basis of the highest similarity of single objects within a cluster. Because the similarity between two elements of two subclusters is sufficient to link them, this criterion can lead to a chaining effect and to large and rather heterogeneous clusters. However, this method is useful in identifying outliers in a group of objects (Everitt, 1974). We used this algorithm in the study reported in Chapter 1 and 2, but compared the resulting cluster structures with cluster structures found with Average Linkage, Ward and *k*-means clustering. In Average linkage the similarity between two subclusters is the average of the similarities between all objects of these clusters. The Ward method combines two groups in a way that within-group heterogeneity increases as little as possible to keep the clusters homogeneous (Ward, 1963). The Ward method and Average Linkage have been shown to provide cluster structures which are a good representation of similarities within the data (Bergs, 1981). In the analyses reported in Chapter 3 and 4 we used Average Linkage and evaluated these cluster solutions further by embedding clusters within a perceptual space found with MDS.

*K*-means clustering is an iterative method which differs from agglomerative clustering in that an object may change its cluster affiliation during the cluster process, when this leads to a decrease in heterogeneity of the cluster structure, while in agglomerative hierarchical clustering cluster assignment of objects is irreversible (McQueen, 1967). The number of clusters extracted with this algorithm has to be specified by the researcher prior to the analysis. Because one aim of our analysis reported in Chapter 1-4 was to identify the number of clusters of respiratory sensations which can be regarded to be distinct, this cluster method was only used to confirm results found with other algorithms.

In all studies reported in Chapter 1-4 we evaluated cluster solutions by embedding clusters within a perceptual space found with MDS. Such a joint presentation is not only useful to evaluate the cluster affiliations found with different cluster algorithms, but can also help to decide on the number of clusters to interpret, as it has been described above (pp. 15-19). Furthermore, we used an elbow criterion similar to the scree-plot in factor analysis to decide on the cluster number to interpret. For displaying a scree-plot, we used the heterogeneity coefficient, i.e. the decrease in heterogeneity on every cluster level, which was related to the specific algorithm we decided to use in the analysis.

To explore the contribution of specific experimental conditions to the formation of specific clusters, so called t-values can be computed per cluster, as reported in Chapter 1. T-values are the mean ratings for an attribute (e.g. breath holding) on the items in one cluster minus the mean ratings for this attribute regarding all items divided by the standard deviation of the attribute-ratings on all items (Backhaus, Erichson, Plinke, & Weiber, 2005, p. 534).

*Comparing MDS configurations found in different groups of individuals*

Scaling and orientation of MDS dimensions are, in the first step, arbitrary. As long as mutual distances remain unchanged, configurations can be rotated to gain a perceptual map with dimensions that can be interpreted in a meaningful way (Kruskal & Wish, 1994). To compare MDS configurations between groups such as between younger and older healthy individuals and individuals suffering from respiratory disease as it has been done in the study reported in Chapter 4, configurations of different groups have to be rotated to an optimal agreement (Peay, 1988). Generalized Procrustes Analysis can be used to orthogonally rotate configurations to an optimal agreement using a least square criterion (Gower, 1975). Procrustes Analysis could also be used to generate one consensus matrix out of several configurations by distorting distances between the objects found in the single matrices. However, in the study presented in Chapter 4 in this report, we used the method only to reach optimal agreement between rotations without changing the relative distances between descriptors. Thus, the real Procrustes act was left out. In doing so, we were able to compare not only the cognitive structure of sensation descriptors, but also the affective evaluation of dyspnea between groups by using Preference Mapping.

*Preference Mapping*

The analysis of similarity ratings via MDS can be expanded to an analysis of preferences (or non-preferences) within a perceptual space via Preference Mapping (Chang & Carroll, 1989). This method is a standard method in economy and marketing research (Schenkman & Joensson, 2000) and has been used in research on the perception of pain (Clark et al., 2001). Here we will describe *external* Preference Mapping only which we applied in the analysis reported in Chapter 4 and not *internal* Preference Mapping, where objects are rated with regard to similarities in preference. In external Preference Mapping, similarities of items and valence (or other characteristics such a frequency of perception) of items are assessed in two separate steps. Preference Mapping allows exploring the contribution of latent dimensions of a perceptual space to valence ratings for the construct in question. In using this method in the analysis reported in Chapter 4, we were able to explore how much variance in discomfort related to dyspnea was explained by different sensory dimensions. By comparing configurations between groups of participants, we were able to compare the contribution of these latent sensory dimensions of dyspnea to affective evaluation of dyspnea between groups.

To model the (non-)preferences of judges for a construct depending on a combination of dimensions, different models have been proposed within the framework of PREFMAP (Chang & Carroll, 1989) that differ in complexity. The simplest model is a vector model:

$$y_k = a_0 + \sum_{r=1}^{R} b_r \, x_{rk}$$

$y_k$ = preference for object k

$x_{rk}$ = coordinate of object k on dimension r (r= 1,…,r)

The coefficients $b_r$ are estimated by linear regression on the basis of preference ratings. The position of a preference vector embedded in a MDS space can be displayed using this regression coefficient $b_r$ (r= 1, …, R). Thus, the vector model of Preference Mapping can be applied using every statistical software package offering regression analysis. In the study reported in Chapter 4, we used the software XLstat (Addinsoft, New York) which creates preference maps and vectors automatically and adjusts the length of vectors in a way that it corresponds to the multiple regression coefficient $R^2$. Projections of descriptor points on such a vector are maximally related to non-preference ratings, i.e. discomfort increase in the direction their vector is pointing (for an example see Figure 4). Using beta-values of the regression coefficient, contributions of the single dimensions of the perceptual space to the affective evaluation of the construct in questions can be explored (see e.g. Schenkman & Joensson, 2000). Vectors can show either valence ratings aggregated across participants in a single vector, or individual valence ratings with one vector per participant. Besides this vector model, other more complex models could be computed, such as the circular ideal point model (Chang & Carroll, 1989). The assumption of this circular model is that the relationship between valence and dimensions of a perceptual space is not linear. For example, the perception of discomfort regarding temperature could be regarded to be u-shaped with very hot and very cold temperatures being perceived as most uncomfortable and moderate temperatures as most comfortable. However, regarding respiratory sensations, we expected latent dimensions of dyspnea to be related in a linear way to associated discomfort. The multiple regression coefficient $R^2$ can serve as index to evaluate the model. It expresses the amount of variance of the preference ratings explained by the dimensions of the perceptual space.

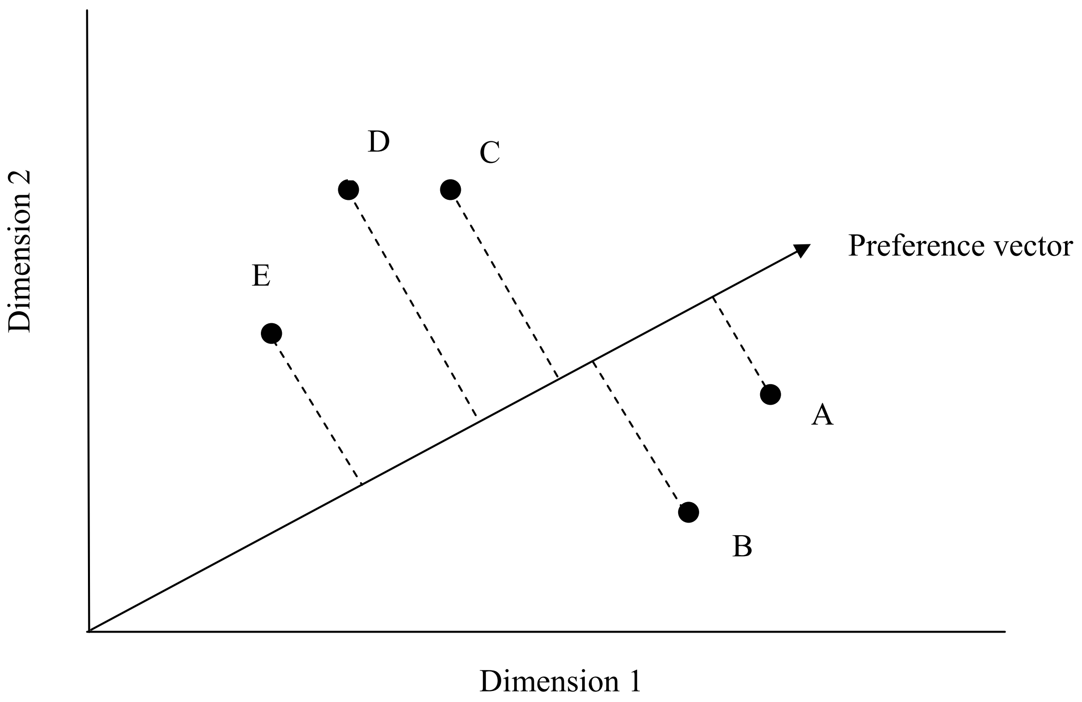


Figure 4: Hypothetical example of a preference vector embedded in a perceptual space. Dotted lines display projections of the object points on this vector. Order of preference ratings should be related as closely as possible to the order of the projection points on the vector.

# CHAPTER 1

## Awareness of Breathing: The Structure of Language Descriptors of Respiratory Sensations

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# Awareness of Breathing: The Structure of Language Descriptors of Respiratory Sensations

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***Objective:*** Recent research suggests that dyspnea is not a single sensation but a multidimensional construct reflected in different verbal descriptors that can provide useful diagnostic information. In this study superordinated clusters of dyspnea were investigated in combination with a dimensional approach. ***Design:*** We examined the use of 20 respiratory symptom descriptors by healthy volunteers who completed a protocol of seven experimental conditions: Quiet breathing, breath holding, paced breathing, climbing stairs, resistive load breathing, voluntary hyperinflation, and voluntary hyperventilation. ***Main Outcome Measures:*** We analyzed the ratings of these descriptors with multidimensional scaling (MDS) and cluster analysis. ***Results and Conclusion:*** While similarities with prior studies were found on a lower fusion level, we were able to demonstrate the usefulness of interpreting higher fusion levels with four clusters related to work of breathing, coordination, suffocation, and struggling for air, merging into two superordinated clusters, effort and air hunger that are compatible with widely accepted primary components of dyspnea. MDS results also suggested that future studies should consider further breathing sensations related to cognitive control of breathing.

*Keywords:* dyspnea, symptom perception, respiratory sensation, verbal descriptors

The perception of breathlessness is an integral part of the symptomatic manifestation of psychological disorders and organic diseases, such as panic disorder, asthma, chronic obstructive pulmonary disease, or cardiopulmonary diseases (Manning and Schwartzstein, 1995; Meuret, White, Ritz, Roth, Hofmann, & Brown, 2006). Research suggests that dyspnea is not a single sensation, but a multidimensional construct that is reflected in language in the use of different descriptors of breathlessness (e.g. Harver, Mahler, Schwartzstein, & Baird, 2000; Mahler, Harver, Lentine, Scott, Beck, & Schwartzstein, 1996; Simon, Schwartzstein, Weiss, Lahive, Fencl, Teghtsoonian, 1989). Three (Perna, Caldirola, Namia, Cucchi, Vanni, & Bellodi, 2004) up to 12 (Elliott, Adams, Cockcroft, MacRae, Murphy, & Guz, 1991) types of dyspnea have been suggested, with a limited overlap between studies of healthy and clinical populations (e.g. Harver et al., 2000; Simon et al., 1989).

While studies on verbal descriptors are variable, physiological analysis suggests that a smaller number of dyspnea components can be distinguished more clearly, a sense of effort, the feeling of hunger for air, chest tightness, and problems not getting enough air (e.g., American Thoracic Society, 1999; Binks, Moosavi, Banzett, & Schwartzstein, 2002; Lansing, Im, Thwing, Legedza, & Banzett, 2000). We suspected that methods used in prior studies of language descriptors may have overestimated both the number of relevant clusters and similarities between healthy and clinical populations. In hierarchical cluster methods, small clusters with one or two items are easier to replicate than larger clusters. Because healthy individuals are less frequently exposed to dyspneic sensations they may actually have less complex concepts of dyspnea. Therefore, by using standard decision rules we sought to determine the number of clusters that could be reasonably discriminated by healthy individuals. Rather than stopping at an earlier fusion level in cluster analysis, as earlier studies did, solutions on a higher level of cluster fusion may be more appropriate. We suspected that if such a solution would be justified, it would converge onto proposed primary components of dyspnea. In addition, by using multidimensional scaling (MDS) we explored whether a dimensional interpretation could offer a more plausible structure compared to an interpretation in terms of discrete clusters of respiratory sensations.

## Method

### Participants

Participants were 14 individuals (12 women, mean age 29.2 years, range 21-41 years), who reported being non-smokers and having no cardiovascular or respiratory disease. They received course credits for their participation. Participants gave consent initially and were then debriefed in detail after the experimental session.

### Instruments

A list of 20 descriptors of respiratory sensations composed by Simon et al. (1989) was translated and adapted to German language (Appendix). Because there is only one counterpart for

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"suffocating" and "smothering" in German language, only one descriptor referring to this sensation was included. As common German expressions we included "I pant for air" and "I am running out of air". A descriptor list closer to the English original would have allowed a comparison between cultures, however, this would have lowered the external validity of such a list for our German sample and our focus was rather on superordinated pattern of sensations than on such an intercultural approach. Each descriptor was rated on a 11-point scale (0 = *not at all*, 10 = *very strong*). Participants also reported on their age, body weight, and medical history in an ad-hoc questionnaire.

### Design and Procedure

The participants completed a protocol of seven conditions varying in intensity and quality of the challenge to the respiratory system: (1) *Quiet sitting*: Participants were instructed to sit quietly with their eyes open for 2 min. They were then asked to rate their respiratory sensations during the task. (2) *Breath holding*: The participants were told to hold their breath for as long as possible. They were then asked to rate how breathless they felt at the moment they started to breathe again. (3) *Paced breathing*: Participants adapted their respiration rate to a pacing tone presented using a tape recorder. Three different speeds were presented, each for 3 min: 8, 13, and18 breaths/min. Following the third and fastest speed, the participants rated their respiratory sensations for this final task period. (4) *Climbing stairs*: Participants climbed a set of stairs to the 7$^{th}$ floor. The instruction was to climb at a steady pace. At arrival on the 7$^{th}$ floor they rated their current respiratory sensations. (5) *Added resistive load breathing*: Participants breathed through a mouthpiece and tube (80 cm, 85 ml deadspace) for 2 min with the nose occluded. An added resistive load (0.75 kPa/l/s) was attached to the distal end of the tube. The experimenter used the digital display of a capnometer to monitor partial pressure of carbon dioxide in the exhaled air (end-tidal $pCO_2$) which had to remain below 45 mmHg. Following the task, participants rated their sensations during the task. (6) *Voluntary hyperinflation*: Participants were instructed to breathe in from resting end-expiratory level to total lung capacity, then to breathe out approximately one-third of the way, and then to continue breathing on that level for 1 min. Afterwards, they rated their respiratory sensations during the task. (7) *Voluntary hyperventilation*: Participants were asked to follow the pacing tone from an audio tape at 18 breaths/min and at the same time breathe with a high tidal volume to reach an end-tidal $pCO_2$ of 20 mmHg (feedback given by the digital display of the capnometer). They were then asked to hold this $pCO_2$ level for 1 min. Following the task they were asked to rate their current respiratory sensations.

The experimental tasks were administered in random order across participants in individual laboratory sessions. Variable breaks between the exercises were given, with a minimum of 10 min after both voluntary hyperventilation and climbing stairs.

### Data Analysis

Before combining judgments to mean ratings for each item per condition, we computed interrater reliabilities (Inter Class Correlations (*ICC*), Shrout & Fleiss, 1979) and excluded descriptors with an $ICC < .75$. Our analysis of the relationships between items was based of the average within-subject structure of each item regarding the seven conditions. Therefore it was important to exclude items for which only low agreement was obtained.

We used two different methods of analysis, cluster analysis using the Single Linkage fusion algorithm and squared Euclidian distances and MDS using squared Euclidian distances. Both methods analyze the relationship between objects on the basis of their mutual similarities or distances with regard to various attributes. In our analysis the seven conditions served as "attributes" and distances between items were computed with reference to the ratings of all seven conditions simultaneously. The decision on the number of clusters to interpret involved two aspects: (i) the homogeneity of the cluster compared to the heterogeneity of the whole group, and (ii) differentiation between clusters (Jardine & Sibson, 1971). Plotting a heterogeneity coefficient as a function of the number of clusters, similar to a scree-plot in factor analysis, it is possible to decide if an earlier fusion level with more and smaller clusters leads to a reasonable increase of homogeneity within the clusters. The second question concerning the differentiation between clusters can be answered by computing a linear discriminant analysis, using the groups of items identified by cluster analysis as input (Méndez, Hödar, Vulpe, González, & Cambiazo, 2002).

In a broader sense MDS can be regarded as a theory of mental stimulus representation (Torgerson, 1958). The scaling algorithm attempts to find a minimum of dimensions that best satisfy the mutual distances between items. Deciding which number of dimensions to choose, the interpretability of the dimensions was taken into account as well as Kruskal's stress formula 1 as a "badness of fit" measure (Kruskal & Wish, 1994). While MDS reveals continuous dimensions that underlie the similarities of objects, cluster analysis displays the degree of similarities between objects in a more particular fashion and combines them into distinct subgroups. Both methods could theoretically be applied to ratings of one person only. Therefore the number of participants was less important, but the number of items and the agreement between participants regarding these items. A heuristic rule of Kruskal and Wish (1994) states that $I\text{-}1 > 4\ R$, where $I$ is the number of stimuli (sensation items) and $R$ the number of dimensions.

A joint representation of MDS and cluster results indicates to what degree these two methods lead to congruent findings (Kruskal & Wish, 1994). The cluster-solution is thereby embedded in the MDS configuration by drawing ellipses around the items of each cluster. A perfect joint representation can only be obtained if clusters can be encircled in such a way that their contours form convex surfaces only and not concave ones (e.g. by loops being forced to slide around one item not belonging to a cluster) and if cluster surfaces do not overlap.

## Results

### Cluster Analysis

Five items with an $ICC < .75$ were identified and excluded: "I feel that I am smothering" ($ICC = .53$), "My chest is constricted" ($ICC = .68$), "I feel that my breath stops" ($ICC = -.07$), "My breathing is shallow" ($ICC = .65$), and "I am running out of air" ($ICC = .44$). Cluster analysis identified four clusters which we interpreted as: 1) *coordination of breathing*, 2) *work of breathing*,

3) *feelings of suffocation*, 4) *struggling for air* (Figure 1). These clusters merge to two superordinate clusters, interpreted as *effort* (cluster 1, 2) and *air hunger* (cluster 3, 4). According to the visual inspection of the dendrogram, a two-cluster-solution would be possible just as well as an eight-cluster-solution including outlier items interpreted as clusters as done in prior research. A scree-plot (not displayed here) showed no further substantial decrease in heterogeneity after a four-cluster-solution. Thus, earlier fusion levels do not lead to more homogeneous clusters. A linear discriminant analysis using the groups recovered by cluster analysis as input showed that the four clusters were statistically separated (*Wilks' lambda* = .16; $chi^2$ (5) = 12.14; $p = .03$).

The Single Linkage algorithm is especially useful for discovering outliers (Jardine & Sibson, 1971). Item 14 (breathing more) joined its cluster very late and item 6 (out of breath) did not join any cluster at all. Item 19 (concentration) also constituted an outlier. It was the only item that described cognitive effort in breathing. After excluding these items, the results of the Single Linkage algorithm were confirmed by the non-hierarchical k-means method which can be regarded as a sign of a stable solution (results can be obtained by request).

### *Interaction of Clusters and Experimental Tasks*

A one-way repeated measure ANOVA of the experimental conditions showed significant differences between quiet sitting and the six tasks that induced respiratory sensation in different ways, $F(6, 66) = 12.40$, $p < .001$, $\eta^2 = .53$. Quiet sitting was rated less intense than the other tasks, post hoc tests (Least Significant Difference) $p < .02$, for five conditions, except breath holding, $p = .30$. The two tasks with the greatest overall intensity were stair climbing and hyperinflation. To display the intensity ratings for each condition separately for each cluster in each condition we computed standardized *t*-values for each experimental task for every cluster. These *t*-values were computed as the difference of the mean condition ratings by one cluster with the mean condition ratings by all clusters divided by the standard deviation of the condition across all clusters (Wishart, 1982). Values near zero indicate that a task contributed little to the formation of this cluster. Negative values indicate that this task has characteristics that are opposite to the cluster characteristics and positive values indicate that the task characteristics are very close to the characteristics of the cluster. Figure 2 displays the interactions between clusters and situations. Hyperinflation shows higher *t*-values for the clusters coordination and work, whereas the *t*-values for stair climbing are higher in struggling for air and lower in suffocation and coordination. Stair climbing and hyperinflation did not differ in their mean dyspnea rating. Thus, clusters seem to be determined primarily by the quality and not by the intensity of dyspnea.

### *Dimensions of Dyspnea Identified in Multidimensional Scaling Analysis*

An ordinal MDS analysis identified three dimensions interpreted as, 1) *need*, 2) *effort*, and 3) *attempt of voluntary control*. Again, items with an $ICC < .75$ were excluded. A stress value of .018 (Kruskal's stress formula 1) indicated an excellent fit for the dimensionality of the data. Figure 3 shows one of the two two-dimensional maps in which the three dimensional configuration was decomposed for the sake of clarity. It displays the dimensions need and attempt of voluntary control. The dimension need ranged between items 13 (tight) and 6 (out of breath). Effort (not displayed here) ranged between items 14 (rapid) and 9 (work) and the dimension, attempt for voluntary control ranged between the items 19 (concentration), and 6 (out of breath). The outlier status of item 14 (rapid), item 6 (out of breath), and item 19 (concentration) which we already observed in cluster analysis, was confirmed in MDS and could be described in more detail regarding the identified dimensions. The first two items described a form of dyspnea

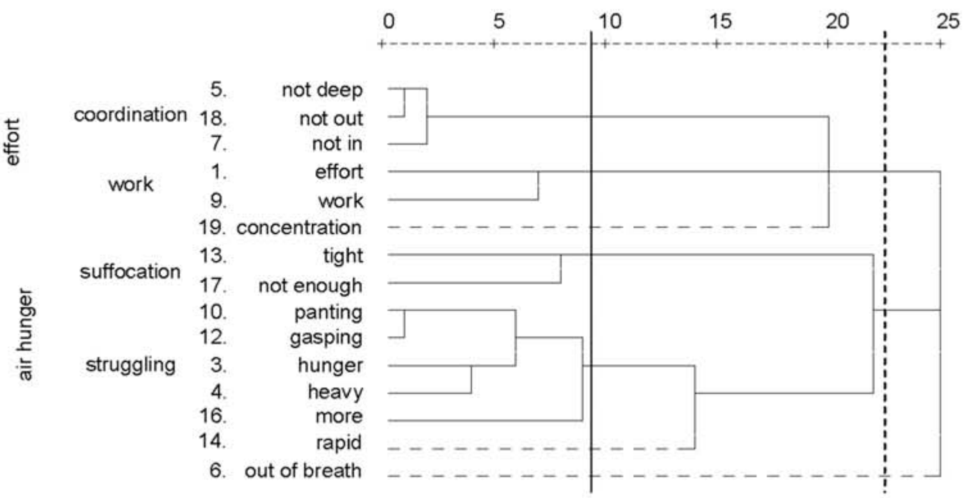


*Figure 1.* Single-linkage dendrogram resulting from hierarchical cluster analysis using squared Euclidian distances. Vertical lines are indicating the fusion levels of the four cluster solution and the superordinated two clusters solution (dashed line). Horizontal dashed lines are indicating outliers.

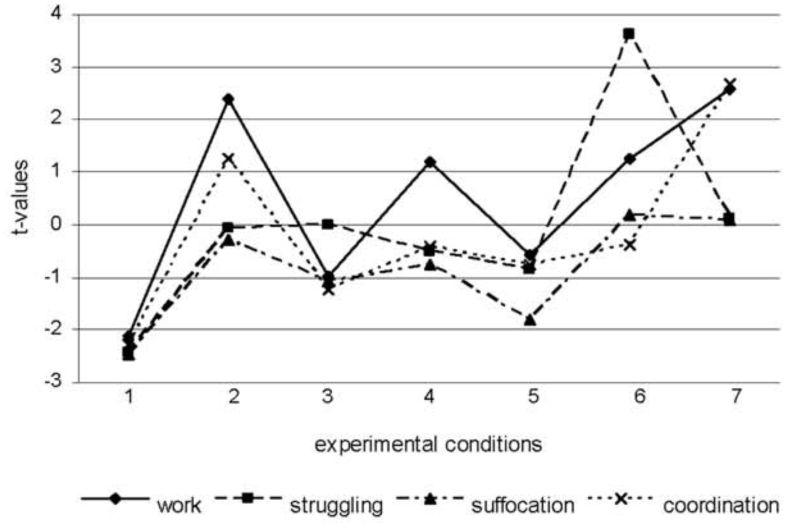


*Figure 2.* T-values of the seven experimental conditions for each of the four clusters: 1) quiet sitting, 2) paced breathing, 3) breath holding, 4) added resistive load breathing, 5) hyperventilation, 6) stair climbing, 7) hyperinflation.

low in need as well as in attempt of voluntary control and effort. In contrast, item 19 ranged from high in attempt of voluntary control over neutral in need to moderately high in effort.

Between an alternative two-dimensional (stress .07) and this three dimensional MDS solution (stress .018) was a substantial decrease in stress, justifying this more complex model. The joint representations (one displayed in Figure 3) showed a good fit between MDS and cluster-solution. The clusters could be embedded in the configurations as clearly separated ellipses which suggested internal validity for the uncovered structure.

### *Discussion*

In this study we explored the structure of the language descriptors of respiratory sensations in healthy individuals. Rather than stopping at a lower fusion level and reporting small but many

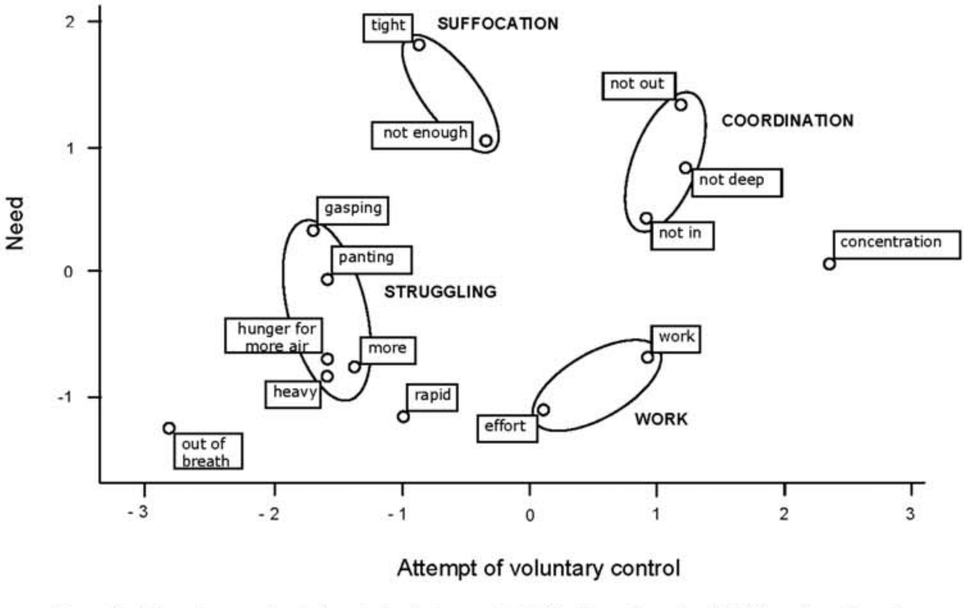


*Figure 3.* Dimensions need and attempt of voluntary control of the three-dimensional MDS configuration using squared Euclidian distances.

clusters, we decided to interpret a solution with four basic clusters that joined into two primary elements of dyspnea effort and air hunger, which is in line with results of physiological analysis (e.g. Binks et al., 2002). We demonstrated sensitivity of these clusters to a range of respiratory challenge tasks depending on quality but not on intensity of induced dyspnea. Interpreting advanced levels of fusion could generate additional information regarding processes that lead from isolated respiratory sensations to more complex forms of dyspnea. Respiratory and cardiopulmonary diseases seem to be associated with a unique set of respiratory sensation clusters (e.g. Manning & Schwartzstein 1995), but more research is needed on the relationship between these clusters and the way in which they converge to primary elements of dyspnea in disease. Future research should explore whether the specific fusion patterns at higher fusion levels differ between healthy and diseased individuals, as well as between different diseases.

A focus on these basic components of respiratory sensation may be more valid for diagnostic purposes. In order to access patients' cognitive representations of symptomatic states, multiple descriptors rather than isolated sensations as suggested by previous cluster solutions may be needed. The coordination cluster for example is constituted by three items related to problems involving breathing in and/or out fully. Healthy individuals are certainly able to differentiate sensations of inhalation and exhalation, but with respect to our respiratory challenge tasks requiring attention to coordination (hyperinflation, i.e. breathing more in than out; and paced breathing, i.e. conscious coordination of inhalation and exhalation) a joint cluster seemed more reasonable. Problems with coordination of breathing related to speech have been observed in clinical conditions such as asthma and chronic obstructive pulmonary (Lee, Friesen, Lambert, & Loudon, 1998; Skevington, Pilaar, Routh, & Macleod, 1997). Items grouped in a coordination of breathing cluster could be specifically sensitive to this aspect of dyspnea.

Our findings with MDS confirmed the integrity of the identified clusters and also emphasize attempt of voluntary control as additional cognitive dimension of dyspnea. Originally, Comroe (1966) identified a dimension "awareness of increased ventilation" in addition to other dimensions of respiratory sensations that were conceptualized more as purely sensory or behavioral. Beyond that, cognitive effort in breathing has largely been ignored. The perceived requirement of controlling breathing actively may constitute an alarm signal similar to increased effort or the need to breathe.

A limitation of our study may have been that the selection of our tasks could have partly determined the outcome of the analysis. The limited role of items of the suffocation subdomain may be suggestive of that. However, similar findings were reported by Simon et al. (1989) who presented their healthy participants with a battery of eight tasks, including $CO_2$ inhalation and resistive load challenge. A larger range of different respiratory challenges, including induced respiratory stimulation or bronchoconstriction with pharmacological agents, may be ecologically more valid elicitors of respiratory sensations for patients (Abelson, Nesse, Weg, & Curtis, 1996). Also the population from which we sampled was a mostly young, healthy student population, thus limiting the generalizability of findings.

Bodily sensations such as dyspnea can only be described sufficiently by the person who experiences it. However, confronted with such a task during an acute illness, patients are often unprepared to provide specific details about their symptoms. A questionnaire detailing aspects of breathlessness could provide patients with guidance to describe and quantify their perceptions more precisely and could help physicians to provide the best diagnosis and treatment. Also, a certain proportion of patients with lung disease have been found to only poorly perceive their internal states, thus making them susceptible to fatal or near-fatal complications (Banzett, Dempsey, O'Donnell, & Wamboldt, 2000). It has been suggested that a dyspnea questionnaire in combination with a methacholine provocation test provoking airway obstruction could serve to identify such "poor perceivers" (De Peuter, Van Diest, Lemaigre, Verleden, Demedts, & Van den Bergh, 2004; Julius, Davenport, & Davenport, 2002). Greater clarity with regard to basic physiologically relevant components of dyspnea would inform this approach. Future studies must also determine the role of emotional states (Rietveld & Prins, 1998) or traits (Chen, Hermann, Rodgers, Oliver-Welker, & Strunk, 2006) in affecting basic aspects of respiratory sensation.

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## Appendix

### List of Respiratory Symptom Descriptors: German Version and English Translation

| German descriptors | English descriptors |
|---|---|
| 1. Meine Atmung erfordert mehr Anstrengung. | My breathing requires more effort. |
| 2. Ich fühle mich als würde ich ersticken.* | I feel that I am smothering. |
| 3. Ich fühle Hunger nach mehr Luft. | I feel a hunger for more air. |
| 4. Ich atme schwer. | My breathing is heavy. |
| 5. Ich kann nicht tief Luft holen. | I cannot take a deep breath. |
| 6. Ich bin auβer Atem. | I feel out of breath. |
| 7. Mein Atem geht nicht den ganzen Weg in die Lunge. | My breathing does not go in all the way. |
| 8. Mein Brustkorb ist eingeschnürt.* | My chest is constricted. |
| 9. Das Atmen erfordert mehr Arbeit. | My breathing requires more work. |
| 10. Ich ringe um mehr Luft. | I am panting for more air. |
| 11. Mir stockt der Atem.* | I feel that my breath stops. |
| 12. Ich schnappe nach Luft. | I am gasping for breath. |
| 13. Meine Brust ist eingeengt. | My chest feels tight. |
| 14. Mein Atem ist schnell. | I feel that my breathing is rapid. |
| 15. Mein Atem ist flach.* | My breathing is shallow. |
| 16. Ich habe das Gefühl ich atme mehr. | I feel that I am breathing more. |
| 17. Ich bekomme nicht genug Luft. | I cannot get enough air. |
| 18. Ich kann nicht genug ausatmen. | My breath does not go out all the way. |
| 19. Meine Atmung erfordert mehr Konzentration. | My breathing requires more concentration. |
| 20. Mir bleibt die Luft weg.* | I am running out of air. |

* Descriptors with an *ICC* < .75 in the German version.

# CHAPTER 2

## Reliability of Verbal Descriptors of Dyspnea and Their Relationship with Perceived Intensity and Unpleasantness

Contributions of the second author: The second author was responsible for the multivariate analysis and interpretation of results obtained with cluster analysis and MDS. Furthermore, general contributions were made to introduction and discussion.

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# Reliability of verbal descriptors of dyspnea and their relationship with perceived intensity and unpleasantness

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*ABSTRACT. Verbal descriptors of dyspnea have been suggested as being useful in providing information on the underlying pathophysiology. However, little is known about the reliability of these descriptors. The present study examined the reliability of a German language list of respiratory symptom descriptors and studied the association of these descriptors with the intensity and unpleasantness of perceived dyspnea. Fourteen healthy volunteers performed cycle-ergometer exercise and voluntary breath-holding during which they rated the perceived intensity (VAS-I) and unpleasantness (VAS-U) of dyspnea on visual analog scales. Following this, they judged their sensations of dyspnea using the list of symptom descriptors. Both conditions were repeated in reverse order on a subsequent occasion 10 days apart. Ventilatory measures, heart rate, blood lactate, VAS-I and VAS-U during cycle-exercise as well as breath-holding time, VAS-I and VAS-U during breath-holding showed no differences between both occasions. Separate hierarchical cluster analyses identified four clusters of verbal descriptors of dyspnea which were widely comparable between both occasions: effort, speed, obstruction and suffocation. Separate multidimensional scaling analyses (MDS) confirmed these four clusters for each occasion. On both days, perceived unpleasantness of dyspnea was correlated with all four clusters during cycle-exercise, while perceived intensity showed only correlations with effort or speed, respectively. No such correlations were obtained for breath-holding. The results suggest that separable clusters of German language descriptors of dyspnea are reliably used by healthy volunteers. The obtained clusters are widely comparable to previously described clusters in other languages and are differently related to the intensity and unpleasantness of perceived dyspnea.*

Key words: *dyspnea, perception, verbal descriptors, diagnosis.*

**RIASSUNTO. MANCA ITALIANO!!!!**

**Parole chiave:** ???.

## Introduction

Dyspnea or breathlessness is an impairing symptom in asthma, COPD and various other cardiovascular or neuromuscular diseases as well as psychological disorders and is associated with severe disability and reductions in quality of life (1-3). Dyspnea is defined as the subjective experience of uncomfortable breathing comprising distinct sensations which can vary in their quality and intensity (1). Hence, it is not a single sensation but rather a multidimensional construct which is also reflected in the language persons use to describe the experienced sensation. Verbal descriptors of dyspnea have therefore been suggested as being useful in providing clinically important diagnostic information on the underlying pathophysiology which might be of further relevance for choosing the optimal treatment of this impairing symptom (4-6).

Recent research on the perception of breathlessness has demonstrated that the feeling of dyspnea consists of at least two primary elements: the sense of work/effort and the feeling of air hunger (1, 7, 8). A number of studies have tried to refine the understanding of these two qualitatively different sensations in healthy persons as well as in different patient groups. Three (6, 9) up to ten (10) distinguishable types of dyspnea have been suggested and partly been linked to specific underlying disease conditions. For example, Simons and colleagues (5) showed that patients with asthma use the terms chest tightness, concentration and exhalation to describe their feelings of dyspnea while patients with COPD preferred the terms hunger, gasping and effort (5). However, little is known to date about the reliability of these descriptors.

Moreover, in analogy to investigations on pain, previous research has demonstrated that the perception of dyspnea also consists of at least two distinct dimensions: a sensory (i.e., intensity) and an affective (i.e., unpleasantness) one. These dimensions can be differentiated during resistive load breathing (11, 12), physical exercise tests (13, 14) or in real life settings (15, 16) by healthy volunteers and by patients with asthma or COPD. How verbal descriptors of dyspnea are related to these dimensions has, however, not been examined yet.

Therefore, the present study examined the reliability of a previously developed German language list of 20 respiratory symptom descriptors adapted from Simon et al. (4) in healthy volunteers who underwent cycle-ergometer exercise and voluntary breath-holding on two separate occasions. Furthermore, the relationship of these descriptors with the intensity and unpleasantness of perceived dyspnea was studied.

## Methods

### Participants

Fourteen healthy volunteers (6 female, mean age = 26.9 years, SD = 4.9) were studied.

Their mean baseline characteristics are summarized in Table I. Acute complaints of the respiratory tract, cardiac failure, pregnancy or any chronic medical conditions, such as asthma or chronic pain were exclusion criteria. After providing informed written consent volunteers underwent a screening spirometry and a resting ECG supervised by a physician. Participants were free to withdraw at any time during the tests. The study protocol was in accordance with the recommendations of the Helsinki Declaration (17).

### Cycle-ergometer exercise

Participants performed incremental cycle-ergometer exercise on an electronically braked ergometer (Excalibur Sport, Lode, Groningen, the Netherlands) to maximum workload with a 25W load increase every 2 min according to the WHO scheme. Tidal volume ($V_T$), minute volume (MV) and breathing frequency (f) were continuously measured with a Metamax spiroergometric system (Cortex Biophysik GmbH, Leipzig, Germany), while heart rate (HR) was continuously monitored with a Polar T 31 heart rate monitor (Büttelborn, Germany). Blood lactate (BL) was sampled at the end of each workload level and analyzed with a lactate analyzing unit applying the enzymatic-amperometric method (Biosen C line, EKF diagnostic GmbH, Barleben, Germany).

### Breath-holding

Participants performed voluntary breath-holding in a sitting position by breathing via a mouthpiece through a breathing circuit with the nose occluded by a clip. After a deep inspiration (i.e., at inspiratory capacity), a shutter was closed which interrupted ventilation. Participants opened the shutter by themselves when dyspnea became intolerable. Breath-holding time ($T_B$) was measured by an experimenter who, for safety reasons, also stopped breath-holding after 2 minutes.

### Measurement of perceived dyspnea

Dyspnea was defined as the sensation of uncomfortable restricted breathing with the connotation that all other sensations (e.g., uncomfortable nose clip or tired legs) are not to be rated. After each experimental condition the experienced degree of intensity (= sensory) and unpleasantness (= affective) was rated on separate visual analog scales (VAS) (18) ranging from 0-10 cm (0 = not noticeable/unpleasant and 10 = maximally imaginable intensity/unpleasant). VAS for intensity (VAS-I) and unpleasantness (VAS-U) were presented in randomised order. The distinct dimensions of perceived dyspnea were explained in detail with standardized examples and the experimenter made sure that the phrases were adequately understood.

A previously developed German language list of 20 respiratory symptom descriptors adapted from Simon et al. (4, 5) (Table II) was presented after the experimental conditions. Each descriptor was rated on a 5-point scale, ranging from 0 (= not at all) to 4 (= very strong). In addition to items used in the English original, we added two items that were more specific to German language expression of respiratory discomfort that can be translated as: "I am running out of air" and "I am panting for more air". In contrast to the English version the German list included only one item describing suffocation directly, because in the German language there is no distinction between smothering and suffocation.

### Experimental Protocol

Before the tests participants were familiarized with all instruments and measurement procedures. In half of the participants this was followed by the cycle-ergometer exercise, in the other half by the voluntary breath-holding test. The experienced respiratory sensations were rated on the verbal descriptor list after each experimental condition, preceded by the visual analog scale ratings of intensity and unpleasantness of dyspnea. After a variable relaxation period the second experimental condition followed with ratings being provided in the same fashion. The same experimental protocol was repeated on a second occasion 10 days later, with cycle-ergometer exercise and breath-holding being presented in reversed order. After the second occasion participants were debriefed.

### Statistical Analysis

Results are reported as means ± standard deviations of the mean (SD). To compare the intensity of cycle-exercise and breath-holding between the two occasions, $V_T$, MV, f, HR, BL, $T_B$, VAS-I and VAS-U were analysed with separate one-way analyses of variance (ANOVA) (occasion 1 vs. occasion 2).

Two different multivariate methods were used for the analysis of the verbal descriptors (separately for each of the two occasions): hierarchical cluster analysis and ordinal multidimensional scaling (MDS). Both are explorative methods analyzing the relationship of objects on the basis of their mutual similarities or distances with regard to various attributes. For both methods, a distance matrix was computed indicating the distance of each item to each of the other items. Both conditions (cycle-exercise, breath-holding) served as "attributes" and the distances were computed with reference to the ratings of the two conditions simultaneously. The aim of cluster analysis is to find homogeneous subgroups of items in the heterogeneous list of descriptors on the basis of the distance matrix. In the present study the Single Linkage algorithm with squared euclidian distances was used and results were confirmed by other fusion algorithms such as Ward and Complete Linkage which can be regarded as a stable cluster solution.

MDS displays the configuration of the items in a multidimensional space on the basis of the square distance matrix. The goal of MDS is to reveal the dimensions that build a perceptual space and the position of each item in this space. The difference between these two very similar methods is that MDS reveals continuous dimensions that underlie the similarities of objects, whereas cluster analysis displays the degree of similarities between the objects more precisely and combines them into distinct subgroups.

The association of perceived intensity and unpleasantness of dyspnea with clusters of descriptors was analyzed by computing rank correlations (Spearman rho, one-tailed) between VAS-I and VAS-U and the clusters, separately for each occasion. All analyses were calculated with SPSS 11.5 software (SPSS Inc., Chicago, IL) using a .05 significance level.

## Results

ANOVAS showed that the intensity of cycle-exercise and breath-holding was comparable between occasion 1 and 2, i.e. no differences in $V_T$, MV, f, HR, BL, $T_B$, VAS-I's and VAS-U's were obtained.

Separate hierarchical cluster analyses identified four clusters of verbal descriptors of dyspnea which were widely comparable between both occasions and which we interpreted as: 1. effort, 2. speed, 3. obstruction and 4. suffocation (Table II). Cluster 1 and 2 as well as cluster 3 and 4 defined two super ordinate clusters: work of breathing and air hunger. However, some descriptors were not located in the same cluster at the second occasion but remained in the super ordinate clusters (grey descriptors in Table II, white and black squares in Figure 1). Only three descriptors were not located in the same super ordinate clusters (bold descriptors in Table II; crosses in Figure 1).

MDS identified two dimensions for both occasions which we interpreted as: work of breathing and air hunger. As a measure of fit Kruskal Stress was used. The two dimensional configuration reached a Stress value of <.005 indicating an excellent fit of the chosen configuration to the data (19). The grouping of descriptors along these dimensions was widely comparable to the results of the clus-

**Table I. *Baseline Characteristics of Participants***

| Characteristics | Data |
|---|---|
| Age (yr) | 26.9 (4.9) |
| Sex (female/male)* | 6/8 |
| Weight (kg) | 73.2 (12.2) |
| Height (cm) | 174.5 (2.2) |
| $FEV_1$ (L) | 3.99 (0.68) |
| $FEV_1$ (% predicted) | 101.5 (11.7) |

* Values are given as No., all other data are presented as mean + (SD).

**Table II. *Schematic overview of the results of the hierarchical cluster analyses and correlation analyses****

| | Cluster | Descriptors at occasion 1 | ρ-VAS-U Cycle-Exercise | ρ-VAS-I Cycle-Exercise | Descriptors at occasion 2 | ρ-VAS-U Cycle-Exercise | ρ-VAS-I Cycle-Exercise |
|---|---|---|---|---|---|---|---|
| Work | Effort | My breathing is heavy.<br>My breathing requires more work.<br>My breathing requires more effort.<br>I feel out of breath. | .51 (p=.032) | .55 (p=.021) | My breathing is heavy.<br>My breathing requires more work.<br>My breathing requires more effort.<br>I feel out of breath. | .57 (p=.017) | .45 (p=.052) |
| | Speed | I feel that I am breathing more.<br>I feel that my breathing is rapid.<br>My breathing is shallow. | .56 (p=.019) | .56 (p=.019) | I feel that I am breathing more.<br>I feel that my breathing is rapid.<br>My breathing is shallow. | .44 (p=.059) | .34 (p=.119) |
| Air Hunger | Obstruction | I am gasping for breath.<br>My chest feels tight.<br>My breath does not go in all the way.<br>My chest is constricted.<br>I feel that my breath stops. | .52 (p=.03) | .38 (p=.09) | **I am gasping for breath.**<br>My chest feels tight.<br>**My breath does not go in all the way.**<br>My chest is constricted.<br>I feel that my breath stops. | .53 (p=.023) | .32 (p=.13) |
| | Suffocation | I feel a hunger for more air.<br>I can not get enough air.<br>I can not take a deep breath.<br>My breathing requires more concentration.<br>I am panting for more air.<br>I feel that I am suffocating.<br>I am running out of air.<br>My breath does not go out all the way. | .47 (p=.045) | .39 (p=.085) | I feel a hunger for more air.<br>I can not get enough air.<br>I can not take a deep breath.<br>**My breathing requires more concentration.**<br>I am panting for more air.<br>I feel that I am suffocating.<br>I am running out of air.<br>My breath does not go out all the way. | .57 (p=.018) | .33 (p=.128) |

* Spearman rho correlations (ρ, one-tailed) between the mean of the item responses of descriptors in each cluster with the VAS ratings of unpleasantness (VAS-U) and intensity (VAS-I) during cycle-exercise for occasion 1 and 2. Four descriptors were not located in the same cluster at the second occasion but remained in the super ordinate clusters (grey descriptors). Only three descriptors were not located in the same super ordinate clusters (bold descriptors).

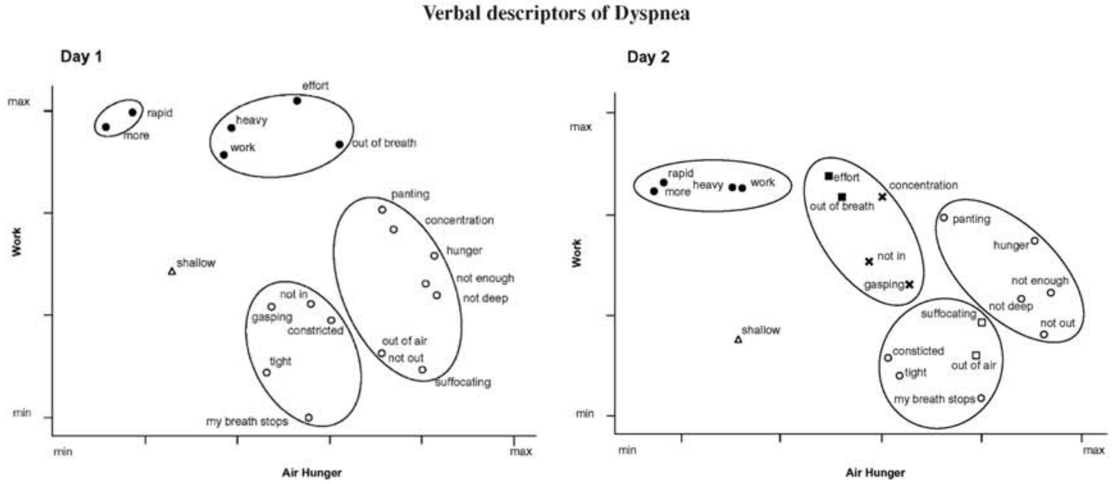


**Figura 1.** ***MDS configuration of descriptors along the dimensions of work and air hunger for the first occasion (left panel) and second occasion (right panel). Black colour indicates descriptors of the super ordinate cluster work of breathing. White colour indicates descriptors of the super ordinate cluster air hunger. White and black squares indicate descriptors migrating between sub clusters within one superordinated cluster, crosses indicate descriptors migrating between the super ordinate clusters, triangles indicate outlying descriptor in MDS***

ter analyses. We displayed the results of MDS and cluster analysis as a joint representation in Figure 1. However, one descriptor ("shallow breathing") was outlying on both occasions.

On both days, perceived unpleasantness of dyspnea showed significant correlations with all four clusters during cycle-exercise, while perceived intensity was only correlated with effort or speed, respectively (Table II). No such correlations were obtained for breath-holding.

## Discussion

In the present study dyspnea was successfully induced in healthy participants by cycle-exercise and breath-holding on two separate days. The intensity of both conditions was comparable between occasions since no differences in physiologic parameters (tidal volume, minute volume, breathing frequency, heart rate and blood lactate) as well as breath-holding time and perceived intensity and unpleasantness of dyspnea were obtained. Results of the hierarchical cluster analyses and the multidimensional scaling showed that four clusters of verbal descriptors of dyspnea could be differentiated by the participants: effort, speed, obstruction and suffocation. The clusters effort and speed as well as the clusters obstruction and suffocation defined two super ordinate clusters: work of breathing and air hunger which is in line with previous findings (1, 7, 8). Perceived unpleasantness of dyspnea showed significant correlations with all four clusters during cycle-exercise, while perceived intensity was only correlated with effort or speed, respectively. In contrast, no such correlations were obtained for breath-holding. Most important for the present study was the finding that these four clusters were widely comparable between both occasions, suggesting that separable clusters of German language descriptors of dyspnea are reliably used by healthy volunteers.

This confirms findings of two recent studies which also reported satisfying test-retest reliabilities of descriptors of respiratory sensations. However, both studies are not directly comparable to the present results. The study by Mahler et al. (10) examined whether patients with COPD choose the same descriptors for their respiratory sensations at rest on two occasions (i.e., recall). Furthermore, they compared the use of descriptors for recalled sensations with the use of descriptors during moderate physical activity. The results showed a 79% agreement of recalled sensations between both occasions and a 68% agreement between recall at rest and physical activity on the second occasion. Since no experimental induction of dyspnea was performed on both occasions to test the reliability of selected descriptors, memory effects might have influenced the obtained results rather than specific physiologic signals. Also Han and colleagues (20) reported a satisfying test-retest reliability of Chinese language symptom descriptors. However, the authors reported only an interval of at least 2 hours between the two ratings which prevents conclusions on the long-term stability of the ratings. Since no acute dyspnea was induced in the study, memory effects might have also influenced the results.

The obtained clusters of descriptors in the present study converge with a number of previous findings. For example, effort of breathing was also obtained in several studies, e.g. Simon et al. (4, 5), Harver et al. (6) and Mahler et al. (10). The speed cluster identified in the present study seems comparable to the fusion of the descriptor "My breathing is rapid" and "I am breathing more" in the studies by Harver et al. (6) and Mahler et al. (10) on a higher fusion level (see respective dendrograms), and also to the factor "rapid breath" in the study of Perna et al. (9)

which combines the descriptors "My breathing is rapid" and "My breathing is shallow". Moreover, the clusters obstruction and suffocation, have also been demonstrated in previous studies (4-6, 21).

An obvious difference between our study and former investigations is the small number of clusters we are restricting ourselves to. In contrast to stopping at a lower fusion level and reporting clusters of only one or two items, we decided to interpret a four cluster solution with rather super ordinate clusters. The rationale of this strategy was based on the finding that these four clusters merge to the two super ordinate clusters "work of breathing" and "air hunger" which have been assumed to be the two primary elements of dyspnea (1, 7, 8). Moreover, these four clusters might mirror recent hypotheses on the underlying physiologic mechanisms for the generation of dyspnea (22, 23). Following this lead, obstruction might be more related to bronchoconstriction and stimulation of pulmonary receptors while suffocation might be closer associated with the stimulation of chemoreceptors (8, 21, 24). Increased effort has been assumed to be related to increased load of the respiratory muscles, stimulation of mechanoreceptors in the chest wall and increased motor command while the speed of breathing could be related to increased motor command or sensory pulmonary or upper airway receptors (24). However, different physiologic pathways might also add or succeed to others and an afferent mismatch, i.e., a dissociation between efferent motor command to the respiratory muscles and afferent feedbacks from pulmonary and chest wall receptors, might be involved in many forms of dyspnea (24). In general, there is no agreement on the specific number of distinct dyspneic sensations resulting in a considerable variety of obtained clusters across studies (25). Therefore, even the number of descriptors within each cluster varies across studies. This might in part be related to the experimental situations during which descriptors were to be rated (e.g., different forms of exercise, hypercapnia, memory). These different contexts might have triggered different physiologic or even psychological pathways and thus have resulted in differences in verbal descriptions.

However, not all descriptors in the present study demonstrated perfect reliability. For example "My breathing requires more effort." and "I feel out of breath." were in the effort cluster on the first, but in the speed cluster on the second occasion. The same holds for the descriptors "I feel that I am suffocating." and "I am running out of air." which were located in the obstruction cluster on the first, but in the suffocation cluster on the second occasion. This might have been caused by their location at the boundaries of the clusters. All four descriptors were, however, located in the same super ordinate cluster work of breathing or air hunger respectively which suggests at least a reliable differentiation of these descriptors between the primary elements of dyspnea. Three descriptors ("My breathing requires more concentration.", "My breath does not go in all the way." and "I am gasping for breath.") migrated between the super ordinate clusters between the two occasions suggesting a limited reliability of these items. This overlaps with findings from Simons et al. (5) who also excluded the items "My breathing requires more concentration." and "I am gasping for breath." as outliers from further analyses. However, future studies are required to establish whether these descriptors show a comparable low reliability in dyspneic patients groups using German language and thus might be excluded in future versions of the descriptor list.

The present study further demonstrated that on both occasions the perceived unpleasantness of dyspnea showed significant correlations with all four clusters of verbal descriptors during cycle-exercise, while perceived intensity was only correlated with effort or speed, respectively. This suggests, that all four clusters of verbal descriptors express to some degree the unpleasant (affective) aspects of perceived dyspnea, i.e., irrespective of the underlying generating mechanism. In contrast, only the descriptors of the super ordinate cluster work of breathing, in particular the effort cluster, seem to mirror the intensity (sensory) aspects of dyspnea. It is tentative to speculate that, therefore, the descriptors related to work of breathing provide more precise information on the underlying pathophysiology than descriptors related to air hunger. This might be further related to differences in the neural and cortical processing between work of breathing and air hunger (26). However, an alternative and rather realistic explanation to date is that we studied healthy participants who normally do not have elaborated experiences with feelings of bronchoconstriction or suffocation. This might have resulted in a specific use of descriptors of the clusters obstruction and suffocation not fully comparable to that of patients suffering from dyspnea. The missing correlations between intensity and unpleasantness of dyspnea and verbal descriptors during voluntary breath-holding might also relate to this circumstance. Since this is the first study relating intensity and unpleasantness of dyspnea to verbal descriptors of this sensation, future studies with an extended experimental protocol and the inclusion of different dyspneic patient samples are clearly required to extend the present findings.

In summary, the present study suggests that separable clusters of German language descriptors of dyspnea are reliably used by healthy volunteers. The obtained clusters effort, speed, obstruction and suffocation are widely comparable to previously described clusters in other languages, but are differently related to the intensity and unpleasantness of dyspnea.

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# CHAPTER 3

## Affective Evaluation and Cognitive Structure of Respiratory Sensations in Healthy Individuals

# Affective evaluation and cognitive structure of respiratory sensations in healthy individuals

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Abstract

*Objective:* Dyspnea is defined as an *uncomfortable* awareness of the need to breathe. However, little is known about the affective evaluation of respiratory sensations in individuals not suffering from respiratory disease. Such knowledge would be important in evaluating the comparability of respiratory sensation report between healthy controls and patient groups.
*Method:* 582 healthy individuals rated 20 descriptors of respiratory sensation with regard to frequency, valence, and situational incidence. Ratings were analyzed on the level of subgroups found with cluster analysis and Multidimensional Scaling.
*Results:* Not all respiratory sensations commonly subsumed under dyspnea are perceived to be uncomfortable by healthy individuals. Two higher-order clusters were found, interpreted as 1) *compensation of dyspnea* and 2) *breathing deficiencies*. Breathing deficiencies were unknown by approximately 50% of participants and rated to be less frequent and more uncomfortable than compensation of dyspnea. Furthermore, three dimensions of respiratory sensations were found using Multidimensional Scaling interpreted as 1) fit between need for air and actual breathing, 2) effort, and 3) attempt of voluntary control.
*Conclusion:* Respiratory sensations are more ambiguous than sensations of other symptom domains such as pain regarding the discomfort they produce. The extent to which respiratory sensation-ratings can be compared between patients and healthy individuals is limited. Latent dimensions of dyspnea might be less affected by differences in interpretation and evaluation of language descriptors of dyspnea and could help to assess comparability of sensation report between groups with different experiential background regarding breathlessness.

**Keywords*:*** dyspnea; health; self-report; respiratory sensation

## Introduction

Sensations elicited by activity of the respiratory system are traditionally analyzed in terms of sensory qualities subsumed under “dyspnea”, such as shortness of breath, air hunger, or effort (e.g. Manning & Schwartzstein,1995; 2001; Scano, Stendardi & Grazzini, 2005), More recently, the importance of the affective component of dyspnea has been recognized because it evokes distress and motivates behaviors such as avoidance of stimuli or seeking help (Banzett, Dempsey, O'Donnell, & Wamboldt, 2000). General intensity and discomfort of dyspnea have been explored in studies using the Borg scale (e.g. von Leupoldt, Ambruzsova, Nordmeyer, Jeske, & Dahme, 2006; Wilson & Jones 1991). Here, discomfort has been shown to be independent from the perceived intensity of dyspnea. Furthermore, using descriptors of emotional states such as being frightened, hopeless, or feelings of lack of energy together with sensory descriptors of dyspnea such as wheezy or short of breath, Skevington et al. (1997) identified a continuum of dyspnea experience ranging from physical to affective qualities in a patient population with respiratory, oncology, or cardiac disease. However, the affective connotation of single physical sensations has not been investigated so far.

Dyspnea is a multidimensional construct with unique sets of qualitatively different sensations that are characteristic for different pathophysiological conditions (Manning & Schwartzstein, 1995; Scano et al., 2005). Analogies between dyspnea and pain, another multidimensional symptom domain (Melzack, 1975), have been drawn in recent research, interpreting dyspnea as a noxious sensation (Evans et al., 2002, Morélot-Pazini et al., 2006; O'Donnell, Chau, Webb,1998; Peiffer, Poline, Thivard, Aubier, Samson , 2001). Discomfort is regarded as an integral quality of pain, “because of unique sensory qualities and because these qualities often occur within a context that is threatening, such as during disease or physical trauma […] and is often accompanied by desires to terminate, reduce, or escape its presence.” (Price, 2000, p. 1796). In line with that, dyspnea has been defined as an uncomfortable awareness of the need to breathe (American Thoracic Society, 1999) and can be an agonizing symptom in a range of somatic and psychological disorders (American Thoracic Society, 1999; Elliott et al., 1991; Mahler et al., 1996; Manning & Schwartzstein, 1995; 2001; Meuret et al., 2006; Perna et al., 2004; Scano et al., 2005; Simon et al., 1990; von Leupoldt et al., 2007). However, in contrast to pain, respiratory sensations occur not only in response to pathophysiological mechanisms and are not only experienced in threatening contexts. Feelings of breathlessness can accompany pleasant activities such as physical activities, sports, meditation exercises, or strong positive emotions. Also, while some respiratory sensation qualities such as air hunger might be perceived as even more uncomfortable than pain by individuals with and without respiratory disease (Banzett & Moosavi, 2001), others might be rather enjoyed by healthy individuals while being perceived as threatening by individuals suffering from a respiratory disease. This implies a wider range of affective evaluations for respiratory sensations than for other physical sensations that are more exclusively related to disease or injury and which are not part of daily life activities in healthy individuals.

In research on dyspnea, healthy samples are often included as control samples or as main target group (Harver, Mahler, Schwartzstein, & Baird, 2000; Petersen, Orth, & Ritz, 2008; Simon et al., 1989; von Leupoldt, Petersen, Scheuchl, & Dahme, 2006). However, little is known about the frequency at which particular qualities of dyspnea are experienced in the daily life of healthy individuals and about the discomfort that is associated with these experiences. The experiential background a person has with regard to respiration, i.e. familiarity, frequency, and situational context of experience of particular sensations can be expected to determine the affective evaluation of particular respiratory sensations. For example, in a study with patients suffering from Chronic Obstructive Pulmonary Disease (COPD), exercise training reduced both the perceived intensity of dyspnea and the associated distress independently from any change in ventilation. The improvement of dyspnea within the exercise program was partly due to a reframing of respiratory sensations as benign and linked to a non-threatening context (Carrieri-Kohlman, Gormley, Douglas, Paul, & Stulbarg, 1996). More knowledge about the affective evaluation of specific respiratory sensations in healthy individuals would be important to clarify the benefits and limits of using healthy samples as comparison groups in clinical dyspnea research. Thus, we sought to explore the affective evaluation of various qualities of respiratory sensations in healthy individuals. We approached this by studying how the affective evaluation of respiratory sensations is linked to their general frequency of occurrence and to the context in which they are experienced.

In addition to types or categories of sensations, we also re-examined the dimensional structure of dyspnea in healthy individuals. The use of a limited number of categories of sensations may be unsatisfactory because "it is not reasonable to expect all people, even if they speak the same language, to link the same word or descriptor to a given sensation. " (Lavietes, 2005, p.1877). While clusters of respiratory sensations have been found to vary on a superordinated cluster level between studies (for a comparison see Garrard & William, 2008) and across repeated assessments in healthy controls (von Leupoldt et al., 2006), latent dimensions of dyspnea report have been found to be stable across studies using experimental induction of dyspnea (Petersen, Orth, & Ritz, 2008; von Leupoldt et al., 2006), or attribute free MDS approaches (Harver et al., 2000). Latent dimensions underlying the formation of categories of respiratory sensations could be less susceptible to between-participant variations in the interpretation and affective evaluation of verbal sensation descriptors. They could also be helpful in assessing the comparability of results of categorical assessments between patients and healthy controls, which have a different experiential background with regard to respiratory sensations.

## Methods

*Participants*

The participants were 582 individuals (155 men), recruited via posters and flyers at the university, but also in other places such as church communities. A paper and pencil as well as an online version of the questionnaire were used. Participants were asked to forward the link to the online questionnaire to friends and relatives. All were of European origin, none reported current respiratory disease. 75 additional participants reporting a history of respiratory disease were excluded from the analyses of this report. We did not offer course credit or other incentives. The opening statements of the survey informed about its background and participation was completely anonymous. The study was approved by the ethic commission of the German Research Society and was carried out in accordance with the American Psychological Association's Ethical Principles.

*Instruments and procedures*

Participants rated 20 descriptors of respiratory sensations that were adapted from a list compiled by Simon and colleagues (1989) and translated into German (Petersen et al., 2008). Ratings were obtained with regard to three aspects asked in three separate sections of the questionnaire: first, general frequency of experience of respiratory sensations, rated on a 5 point scale (0=*never*/ 4=*frequent*) and second, on a separated page, discomfort associated with sensations, (0=*very pleasant*/ 4=*very uncomfortable,* 5=*"not applicable"*). Finally, also on a separate page, participants indicated for each sensation the situation in which they would mostly experience it, (i) *sport and exercise*, (ii) *emotion and stress*, (iii) *somatic disease* (not restricted to chronic disease), (iv) *others (not specified),* or (v) *unknown*. Here, multiple answers were possible in a yes/no format. If 'others' was selected, the instruction was to specify the situation in free response format. Additional demographic and health related information was collected at the end of the questionnaire such as smoking habits and self-reported diagnosis of any respiratory complaints.

*Data Analysis*

To explore the structure of respiratory sensations we identified groups of descriptors by using cluster analysis (Average Linkage) and computed an ordinal MDS. Because we analyzed frequencies, the Chi² metric was used. We used Kruskal's algorithms to estimate goodness of fit, or "stress" of the MDS configuration. As a convention, a stress value of .05 can be regarded as good fit index, .025 as excellent. All analysis except the canonical correlation analysis described below were computed using the software XLstat (Addinsoft, New York). MDS and cluster analysis have been developed as theories of perception and are rooted in the tradition of psychophysical research (e.g. Torgerson, 1958). They offer the advantage of exploring the dimensions and types of dyspnea by including *multiple* aspects of dyspnea *simultaneously,* for instance to explore dyspnea experienced in response to different stimuli or in different situations simultaneously in one analysis (Kruskal & Whish, 1994). Traditionally, because the perception of dyspnea can arise in response to a multitude of different mechanisms, cluster analysis and MDS have been the preferred methods in most studies on the report of dyspnea (Elliott et al., 1991; Harver et al., 2000; Mahler et al., 1996; Petersen et al., 2008; Simon et al., 1989; 1990; von Leupoldt et al., 2007; 2006).

Everitt (1974) and Kruskal and Wish (1994) have suggested combining the analysis of clusters with a dimensional approach such as MDS. The combination of these methods can help to assess the number of clusters that should be interpreted. Furthermore, the additional information an MDS configuration provides on latent dimensions of dyspnea can help improve the interpretation of sensation clusters. We used MDS to define sensation descriptors as n-dimensional coordinate in an n-dimensional space. Clusters found with hierarchical clustering should constitute regions in this space with a relative high density of points separated from other such regions by areas with a relative low density of points. Clusters described in this way are sometimes referred to as *natural clusters* (Everitt, 1994, p. 44). The optimal number of distinct types of dyspnea in terms of such natural clusters has not been assessed so far. It could be assumed that a smaller number of such natural categories can be found as suggested by recent research.

To investigate differences between sensations in frequency and discomfort, we restricted the analyses to the cluster level. One-way repeated measures analyses of variance (ANOVA) were calculated separately for frequency and discomfort ratings, in which levels of the within-subject variables were the identified clusters and outlier-items without cluster affiliation. Partial eta-square ($\eta^2$) was calculated as the measure of effect size. Bonferroni corrected *t*-tests were performed to explore differences between single cluster pairs.

The association of respiratory sensations with the demographic and health-related variables was studied using canonical correlation analysis (CANCORR macro, Advanced Statistic Module of SPSS). Canonical correlation simultaneously predicts multiple dependent variables from multiple independent metric or non-metric variables. For this purpose, canonical loadings for each variable of the two sets are interpreted similar to factor loadings in factor analysis (Hair, Anderson, Tatham, & Black, 1998).

## Results

### *Participant's characteristics*

The age of respondents ranged between 15 and 89 years, with a mean±SD age of 29.2±11.4 years. All were of European origin and none of them reported having respiratory disease. 75 further participants reporting a history of respiratory disease were excluded from the analyses of this report. Current smoking was reported by 157 participants (36 men) and regular smoking at least once in the past by 223 (66 men), with the mean number of cigarettes of 5.5 ±8.4 and the mean duration of smoking of 100.2±78.0 months. The mean pack year index was 2.60±5.77. The body mass index (BMI) of the whole sample ranged between 16.4 and 40.6 (mean BMI=22.3±3.1), with 12 participants (7 men) being adipose (BMI≥30). The mean value for physical activity was 1.32±1.03, indicating that the average level of activity in our sample could be described as exercise or sport only on the weekend or during holidays. Gender differences were only found for BMI ($p$<.001) with a mean BMI for men of 24.5±3.03 and 21.6±2.90 for women, but not for physical activity, age, or pack year index. No significant differences between ratings obtained with the paper and pencil (N=380) and the online questionnaire (N=202) were observed on the level of mean scores for clusters tested with $t$-tests (all $t$ (580) < 1.272).

*Frequency of experience and associated discomfort*

Respiratory sensations varied with regard to frequency of experience and associated discomfort as well as situational incidence. Means and standard deviations and percentages of assignments of respiratory sensations to rating categories are shown in Table 1. Even the sensation rated to be most frequent ("I am out of breath") was rated to occur only seldom (mean rating 2.0±1.1). Mean discomfort ratings ranged from "a little pleasant"("breathing more", mean rating 1.74±1.01) to "very uncomfortable". The sensation described by the item with the highest average discomfort rating across participants ("suffocating") with a mean of 3.81±0.50 was rated to be never experienced by 74.0% of our participants.

#######Please insert Table 1 about here########

*Structure of respiratory sensations found in cluster analysis and MDS*

We found a cluster structure with two main groups of descriptors which we interpreted as 1) *compensation of dyspnea* and 2) *breathing deficiencies.* These clusters were further divided into five subclusters and two outliers. The sub-clusters 1) *work,* the two-item cluster 2) *concentration/hunger,* and the sub-cluster 3) *struggling for air* constituted the cluster compensation of dyspnea. The clusters 4) *problems with coordination of inhalation and exhalation* (here referred to as *coordination*)*,* 5) *obstruction,* and the outliers "I feel that my breath stops" and "I am running out of air" constituted the cluster of deficiencies in breathing (Figure 1). To gain a deeper understanding of this cluster structure, we explored further the dimensional structure of respiratory sensations by MDS. We found three dimensions (Kruskal's stress .02 which can be regarded as excellent fit) that were interpreted as 1) *fit between need for air and breathing* (here referred to as *fit* dimension)*,* 2) *effort,* and 3) *attempt of voluntary control* (ranging between the items "My breathing requires concentration" and "I am out of breath", not displayed)

Figure 2 shows clusters embedded in the MDS configuration, displaying projections of the positions of descriptors on the two dimensions of effort and fit. This joint presentation can be regarded as an internal validation of the two explorative methods. Clusters found with hierarchical cluster analysis were not overlapping when embedded in the MDS configuration but constituting distinct partitions (Kruskal & Wish, 1994), i.e. both methods were identifying the same groups of sensations. This way MDS confirmed the decision on a rather small number of clusters. Choosing more clusters would have led to clusters that would not have constituted clearly separated groups within the MDS configuration. Furthermore, this joint presentation gives additional help in interpreting cluster structures according to their location in the area of the MDS configuration characterised by good or poor fit and high or low effort.

#######Please insert Figure 1 about here########

Cluster-means and post-hoc tests of single cluster pairs can be found in Table 2. None of the clusters' means for frequency was higher than 1.4 (struggling for air), indicating that all types of dyspnea were experienced "very seldom" or "seldom" by healthy individuals. All clusters were associated with substantial discomfort. However, comparing the two main groups of descriptors, we found that *compensation of dyspnea* was experienced more often than *deficiencies in breathing*, $F(1,581)=171.96$, $p<.001$, $\eta^2=.228$, and was associated with less discomfort, $F(1,552)=305.63$, $p<.001$, $\eta^2=.356$.

Regarding the number of participants indicating they had never experienced a certain sensation, these ratings were lower in subordinate clusters of compensation of dyspnea (28.4%, 39.3%, and 32.9%, for struggling for air, work, and concentration/hunger, respectively) than for subordinate clusters/items of deficiencies in breathing (49.2%, 52.3%, 40.8, and 74.0%, for coordination, obstruction, "My breath stops" and "I am running out of air", respectively). McNemar *Chi²* test revealed that the ten items of the superordinated descriptor group breathing deficiencies were significantly more often rated to be unknown to participants than the ten descriptors of the superordinated group compensation of dyspnea, McNemar $\chi^2(1)=600.46$, $p<.001$.

Figure 3 shows the absolute number of assignments of central items for each subcluster to the categories *exercise*, *stress/emotions*, *disease*, *others* and *unknown*. The cluster of struggling for air ("rapid") was mostly related to situations of exercise and, to a smaller extent, to stress but not to disease. The cluster for work of breathing ("effort") was also mostly experienced during physical activity. Concentration/ air hunger ("concentration") were mostly relevant during exercise and stress. Items of the superordinated cluster deficiencies in breathing (obstruction: "tight", coordination: "not in") were assigned to the category "unknown" by most participants, except for the two outliers that were related mostly to stress/emotion.

#######Please insert Figure 2 about here########

To analyze a potential association of age, gender, BMI, smoking habits, and exercise habits with the report subgroups of respiratory sensations, we computed a canonical correlation analysis. We found only one significant canonical functions for frequency ratings (Function 1: $Rc$=.244, $\chi^2(35)=58.63$, $p$=.007, Function 2: $Rc$=.171, $\chi^2(24)= 28.51$, $p$=.239, all other functions $\chi^2<13.87$) and no significant canonical function for discomfort associated with different qualities of respiratory sensations (Function 1: $Rc$=.354, $\chi^2(35)=43.81$, $p$=.146, all other functions $\chi^2<16.61$) (see Table 3 for canonical loadings). We interpreted the first canonical function for frequency as *physical fitness*. It was characterized by high positive loadings for physical activity/exercise and male gender, together with moderate negative loadings for smoking, together with negative loadings for all clusters, especially high for obstruction and the two outliers. The canonical function for discomfort was characterized by a high positive loading for age, and a moderate loading for male gender, together with a substantial negative loading for work and concentration, and a small negative loading for coordination, but a small positive loading for the outlier item "My breath stops". We interpreted this canonical function *as age-related stoicism towards dyspnea-related discomfort*. It must be noted that the model fit index for the canonical function for discomfort was poor, thus, the function must be interpreted with care only.

###### Please insert Table 3 about here #####

## Discussion

Self-report on the quality of a bodily experience can provide useful information with regard to underlying physiological and pathophysiological mechanisms. However, experiential qualities can only be measured by the self-report of the person who is experiencing them. The validity of sensation report as a reflection of physiological change can only be evaluated after clarifying the meaning the individual assigns to verbal sensation descriptors. This meaning at least partly depends on the affective evaluation of sensations. Our results suggest that the affective evaluation of different types of dyspnea by healthy individuals varies substantially and is related to familiarity with a sensation and context of experience. Not all respiratory sensations commonly subsumed under dyspnea (which is defined as an uncomfortable awareness of breathing) are necessarily perceived as uncomfortable in health. This limits the comparability of sensation ratings between individuals with and without known respiratory disease. Controlling for affective evaluation could help to clarify whether respiratory sensations reported by different groups in response to the same stimulus are comparable.

Using cluster analysis initially, we found two superordinated clusters of respiratory sensations for our healthy sample which were interpreted as compensation of breathing and breathing deficiencies. These superordinated clusters seemed to bear some resemblance to major clusters of sensations identified for patients in respiratory medicine, which are sensations of effort that are mainly related to respiratory muscle activity, and air hunger and obstruction that are mainly related to a number of other mechanisms such as the stimulation of chemical, irritant, and sensory receptors (Binks, Moosavi, Banzett, & Schwartzstein, 2002; Lansing, Im, Thwing, Legedza, & Banzett, 2000; Moy, Woodrow-Weiss, Sparrow, Israel, & Schwartzstein, 2000). We chose these alternative labels to emphasize the potential differences in interpretation of these verbal descriptors in individuals without known respiratory disease rather than to state differences in underlying physiological mechanisms. For individuals without respiratory disease, the different degrees of control over various aspects of dyspnea could be the main factor for categorizing and evaluating respiratory sensations.

Compensation of dyspnea was characterized by a good to acceptable fit between need for air and actual breathing. Sensation items subsumed under this group were perceived to be less uncomfortable than breathing deficiencies with one item even being in the pleasant affective range (“ I feel that I am breathing more”). The affective evaluation of sensation descriptors was also related to the context of experience. Items subsumed under compensation of dyspnea were experienced mainly during exercise and, only to a smaller extent, during disease or stress and emotion. In contrast, the second group of items labelled “breathing deficiencies” encompassed items that suggested a potentially enduring impediment to breathing or mismatch between ventilation and metabolic demand which were clearly perceived as unpleasant also by healthy individuals. Only this group of sensation descriptors can be interpreted to constitute a “core-dyspnea” in healthy individuals in accordance with the definition of dyspnea as uncomfortable awareness of breathing (American Thoracic Society, 1999). An important characteristic of this cluster was that respiratory sensations subsumed under it were unknown to approximately 50% of our sample and mostly associated to strong emotions and stress for the remaining sample. Thus, our results suggest that dyspnea in terms of an uncomfortable awareness of breathing is restricted to a small number of sensations in individuals without pulmonary disease. Some of these sensations that are typical for patients may be unknown to most non-patients having a more exclusive affiliation with bronchoconstriction in respiratory disease (e.g. Banzett et al., 2000) or respiratory conditions that otherwise healthy individuals cannot easily overcome, such as hyperventilation (Grossman, de Swart, & Defares, 1985). These sensations might never be perceived by healthy individuals in daily life or in the laboratory, except for in extreme situations or in response to extreme stimuli.

Items subsumed under compensation of dyspnea have been found to be related to pathophysiological processes in respiratory disease such as the sensation of effort to COPD

(O'Donnell et al., 2007). Effort is perceived as highly uncomfortable and threatening by individuals suffering from COPD or asthma but as unthreatening by healthy individuals as long as blood gas levels remain normal (Banzett et al., 2000). Thus, in research that includes healthy individuals, ratings of sensations subsumed under the compensation of dyspnea cluster should be interpreted with care and are not necessarily comparable with ratings of patient populations. Ratings of the affective evaluation of respiratory sensations could help in comparing dyspnea ratings between populations with different experiential backgrounds across health and disease. Additionally, familiarity with sensations should be checked routinely in such research.

In a subsequent MDS analysis, we found meaningful dimensions underlying the experience of dyspnea in healthy individuals which were 1) fit between need for air and actual breathing, 2) effort, and 3) attempt of voluntary control. Displaying respiratory sensations in a perceptual space found with MDS helped to interpret sensation clusters and to decide on the number of clusters. Furthermore, while our results suggest that we cannot automatically assume that dyspnea categories have the same meaning in patients as they have in healthy individuals, more research is needed on dimensions underlying dyspnea in individuals suffering from respiratory disease. Latent dimensions of dyspnea have been found to be stable across repeated assessments in one study (von Leupoldt et al., 2006) and across studies that have included varying numbers of respiratory sensation descriptors and different methods of assessment, e.g. response to experimental induction of dyspnea (Petersen et al., 2008), attribute free approaches (Harver et al., 2000), or retrospective report as utilized in the present study. In contrast to latent dimensions of dyspnea, cluster solutions are more dependent on individual differences in interpretation and affective evaluation of sensations. Cluster analysis is also more sensitive to individual items included in an analysis. This can become problematic because there is no consensus on a list of definitely important sensation items. In analyzing the structure of dyspnea, sensation lists of fifteen (Harver et al., 2000) up to forty-five (Elliott et al., 1991) sensations have been found useful in research. However, patients themselves use a higher number of descriptors. Skevington et al. (1997) found that patients with respiratory disease, cardiac disease, or cancer used 63 different sensation items to describe their symptoms. Parents have been found to name 136 unique symptoms to describe asthma they observe in their children (Yoos, Kitzman, McMullen, Sidora-Arcoleo, & Anson, 2005). Studies have also found cultural differences in symptom descriptions (Han et al., 2005; 2008, Hardie, Janson, Gold, Carrieri-Kohlman, & Boushey, 2000). On the other hand, latent dimensions could reveal the more general cognitive structure of sensation that is less affected by cultural and individual differences in the understanding of language descriptors or the composition of symptom lists used. Latent dimensions of dyspnea could provide a more global, shared reference system to compare dyspnea experiences between patient groups and healthy controls.

In using canonical correlation analysis, we found demographic and health related variables to have only small influence on the report of respiratory sensations. Regarding gender, our canonical correlation analysis showed for male participants less frequent reports of breathing deficiencies, but not of compensation of dyspnea. Prior research has shown that men typically report respiratory symptoms such as asthma symptoms to be less frequent and less severe compared to women (e.g. Ritz, Bobb, Edwards, & Steptoe, 2005). Our results confirm this tendency. However, it should be noted that the small size of the canonical correlations showed that such gender differences explain only little variance in respiratory symptom reports.

Our study was limited in that psychological factors that have been shown to influence retrospective symptom report, such as trait negative affect (Watson & Pennebaker, 1989), were not included in our study. Controlling for negative affect might have influenced our results, in particular regarding the breathing deficiencies cluster that was more strongly related to situations of stress and disease than the compensation of dyspnea cluster. However, the good comparison with our earlier study in which we induced dyspnea experimentally (Petersen et al., 2008) shows that the distinctions healthy individuals make between qualities are reproducible beyond assessment contexts and are reminiscent of meaningful distinctions between sensation qualities in basic respiratory physiology and respiratory medicine.

*Conclusion*

Respiratory sensations show a wide range of affective evaluations on the pleasantness-unpleasantness continuum. Core-dyspnea in terms of a clearly unpleasant awareness of breathing occurs rarely in healthy individuals. Methods to induce dyspnea in experimental research including healthy control samples should be chosen carefully regarding possible differences in compensability of induced dyspnea for individuals with and without respiratory. Comparisons of sensation reports with clinical groups should be made with care, especially for sensation items which are potentially ambiguous with regard to their pathological character.

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*Conflict of interest*

None of the authors has a conflict of interest.

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Table 1. Mean frequency of experience and discomfort associated with respiratory sensations in healthy individuals ($N = 582$), standard deviation in parentheses, with percentage of ratings for the five answer-categories for frequency and discomfort.

| | Frequency | Discomfort | % Frequency ratings | | | | | % Discomfort ratings | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 0 | 1 | 2 | 3 | 4 | 0 | 1 | 2 | 3 | 4 |
| I feel out of breath. | 2.01(1.05) | 2.69(0.83) | 9.66 | 21.90 | 30.69 | 33.79 | 3.97 | 0.93 | 8.52 | 23.33 | 55.00 | 12.22 |
| My breathing is rapid. | 1.92(1.11) | 2.54(0.79) | 10.86 | 28.79 | 22.41 | 33.45 | 4.48 | 0.76 | 9.56 | 31.17 | 51.82 | 6.69 |
| My breathing is shallow. | 1.82(1.21) | 2.60(0.92) | 33.56 | 41.00 | 15.22 | 10.03 | 0.17 | 1.03 | 3.87 | 11.60 | 63.66 | 19.85 |
| I have the feeling I am breathing more. | 1.21(1.16) | 1.74(1.02) | 35.24 | 42.01 | 15.63 | 6.77 | 0.35 | 1.16 | 3.24 | 12.04 | 63.66 | 19.91 |
| I feel hunger for air. | 1.10(1.13) | 2.90(0.89) | 15.77 | 27.73 | 23.74 | 24.44 | 8.32 | 2.33 | 11.65 | 21.19 | 53.39 | 11.44 |
| My breathing requires more effort. | 1.02(0.95) | 2.97(0.75) | 34.20 | 41.11 | 14.68 | 9.15 | 0.86 | 0.73 | 4.12 | 7.99 | 54.00 | 33.17 |
| I am gasping for breath. | 1.01(0.97) | 3.15(0.79) | 48.45 | 31.44 | 14.09 | 5.84 | 0.17 | 0.27 | 1.62 | 4.59 | 52.70 | 40.81 |
| My breathing does no go in all the way. | 1.01(1.15) | 3.10(0.63) | 47.31 | 30.85 | 13.34 | 7.80 | 0.69 | 0.88 | 3.54 | 10.91 | 63.13 | 21.53 |
| My breathing is heavy. | 0.95(0.90) | 2.98(0.74) | 35.98 | 27.16 | 18.34 | 16.58 | 1.94 | 10.45 | 33.90 | 30.79 | 21.19 | 3.67 |
| My breath stops. | 0.94(0.95) | 3.23(0.63) | 40.76 | 39.38 | 10.02 | 8.81 | 1.04 | 0.74 | 0.74 | 1.24 | 27.23 | 70.05 |
| I cannot get enough air. | 0.90(0.97) | 3.65(0.62) | 38.58 | 30.62 | 14.53 | 14.36 | 1.90 | 1.35 | 7.57 | 14.32 | 53.51 | 23.24 |
| My breathing requires more work. | 0.84(0.98) | 3.01(0.74) | 47.84 | 33.16 | 11.23 | 6.39 | 1.38 | 0.81 | 1.08 | 2.43 | 55.41 | 40.27 |
| I cannot take a deep breath. | 0.80(0.97) | 3.33(0.66) | 52.33 | 27.98 | 10.71 | 7.94 | 1.04 | 1.24 | 5.57 | 23.53 | 56.04 | 13.62 |
| I pant for breath. | 0.78(0.91) | 3.32(0.66) | 37.89 | 39.10 | 14.01 | 8.65 | 0.35 | 0.53 | 0.53 | 6.38 | 60.90 | 31.65 |
| My chest feels tight. | 0.78(0.96) | 3.52(0.61) | 44.73 | 27.29 | 12.61 | 12.61 | 2.76 | 0.32 | 0.32 | 12.50 | 63.14 | 23.72 |
| My breathing requires more concentration. | 0.77(1.00) | 2.75(0.80) | 50.00 | 31.38 | 10.34 | 7.59 | 0.69 | 0.64 | 1.93 | 0.00 | 41.80 | 55.63 |
| I am running out of air. | 0.64(0.83) | 3.52(0.68) | 54.47 | 31.44 | 9.97 | 3.95 | 0.17 | 0.63 | 1.27 | 3.16 | 35.44 | 59.49 |
| My chest feels constricted. | 0.63(0.87) | 3.62(0.62) | 57.02 | 28.77 | 9.19 | 4.33 | 0.69 | 0.69 | 0.69 | 1.04 | 31.49 | 66.09 |
| My breathing does not go out all the way | 0.62(0.89) | 3.35(0.65) | 58.45 | 27.41 | 8.45 | 5.00 | 0.69 | 0.40 | 0.80 | 5.20 | 50.80 | 42.80 |
| I feel that I am suffocating | 0.36(0.71) | 3.81(0.50) | 74.04 | 18.64 | 4.53 | 2.44 | 0.35 | 0.46 | 0.00 | 1.83 | 13.70 | 84.02 |

Table 2. Means of cluster ratings and post hoc comparisons (Bonferroni corrected *t*-tests)

| | | Significance of difference between cluster ratings | | | | | |
|---|---|---|---|---|---|---|---|
| | Frequency | 1. | 2. | 3. | 4. | 5. | 6. |
| 1. Struggling for breath | 1.39(.70) | | | | | | |
| 2. „My breath stops“ | .94(.95) | <.001 | | | | | |
| 3. Concentration/ hunger | .94(.86) | <.001 | >.900 | | | | |
| 4. Work | .94(.75) | <.001 | >.900 | >.900 | | | |
| 5. Obstruction | .90(.67) | <.001 | >.900 | >.900 | >.900 | | |
| 6. Coordination | .83(.77) | <.001 | .147 | .023 | .007 | .321 | |
| 7. „I am running out of air“ | .64(.83) | <.001 | <.001 | <.001 | <.001 | <.001 | <.001 |
| | Discomfort | 1. | 2. | 3. | 4. | 5. | 6. |
| 1. Struggling for breath | 2.74(.60) | | | | | | |
| 2. „My breath stops“ | 3.23(.64) | <.001 | | | | | |
| 3. Concentration/ hunger | 2.87(.73) | .115 | <.001 | | | | |
| 4. Work | 2.95 (.57) | <.001 | <.001 | .095 | | | |
| 5. Obstruction | 3.39(.47) | <.001 | <.001 | <.001 | <.001 | | |
| 6. Coordination | 3.37(.52) | <.001 | .002 | <.001 | <.001 | >.900 | |
| 7. „I am running out of air“ | 3.56(.66) | <.001 | <.001 | <.001 | <.001 | <.001 | <.001 |

Table 3. Canonical structure for the canonical function for frequency of experience and discomfort.

| | Canonical loadings | |
|---|---|---|
| | Frequency | Discomfort |
| | Function 1: Physical fitness | Function 1: Stoicism |
| Gender | .702 | .440 |
| Age | .085 | .854 |
| Sport and exercise | .583 | .091 |
| Pack years | -.387 | -.041 |
| BMI | .230 | .377 |
| Work | -.470 | -.742 |
| Concentration | -.324 | -.670 |
| Struggling for air | -.164 | -.040 |
| Obstruction | -.801 | -.060 |
| Coordination | -.430 | -.277 |
| “My breath stops” | -.654 | .260 |
| “I am running out of breath” | -.538 | .052 |

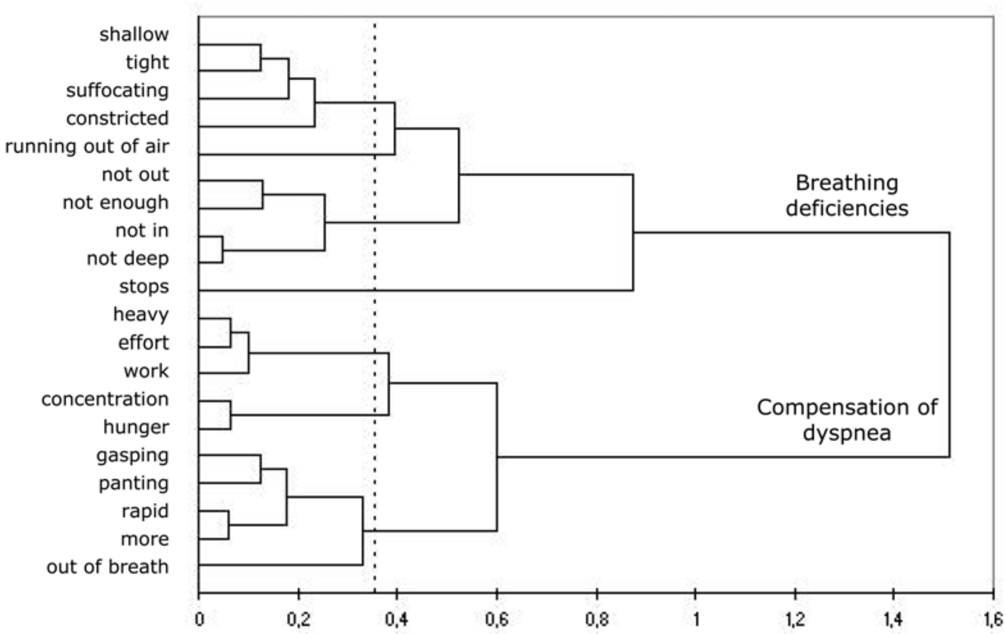
**Figure captions**

Figure 1. Dendrogram (Average Linkage, Chi² Metric) displaying fusion of 20 descriptors of respiratory sensations into clusters.

Figure 2. Joint representation of clusters of respiratory sensations within MDS configuration.

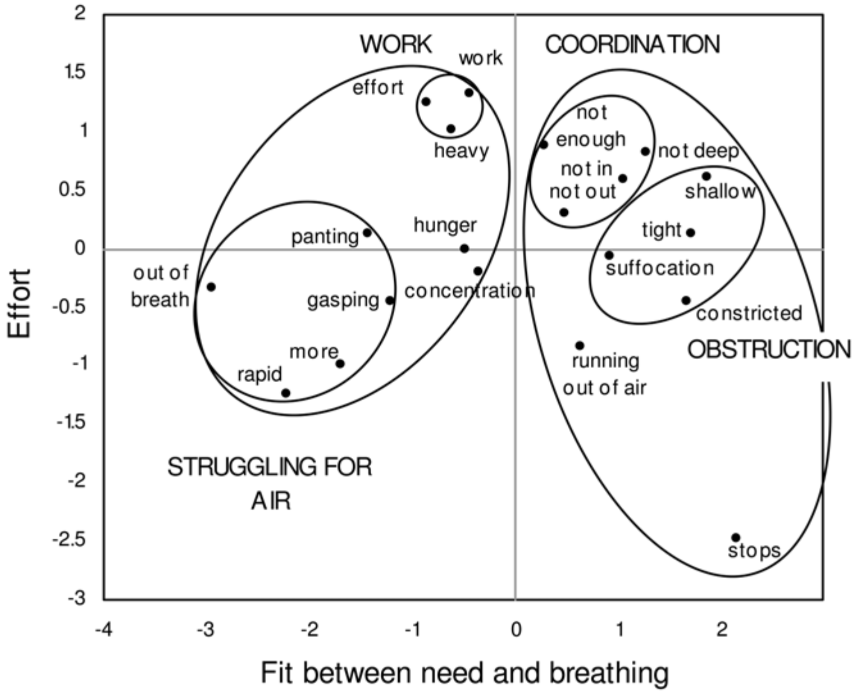
Figure 3. Assignment of central cluster items to the four categories 1) exercise, 2) stress/ emotions, 2) disease, 3) other situations and 4) unknown.

Figure 1



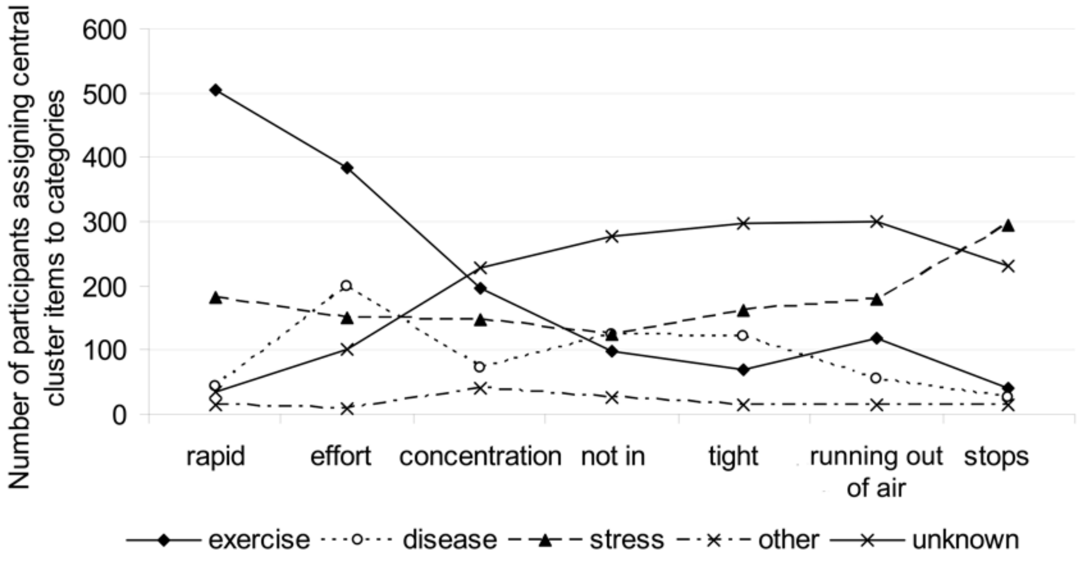
shallow
tight
suffocating
constricted
running out of air
not out
not enough
not in
not deep
stops
heavy
effort
work
concentration
hunger
gasping
panting
rapid
more
out of breath
Breathing deficiencies
Compensation of dyspnea
0
0,2
0,4
0,6
0,8
1
1,2
1,4
1,6

Figure 2



WORK
work
effort
heavy
COORDINATION
not
enough
not in
not out
not deep
shallow
tight
suffocation
constricted
OBSTRUCTION
running
out of air
stops
hunger
concentration
panting
out of
breath
gasping
more
rapid
STRUGGLING FOR
AIR
Effort
Fit between need and breathing
2
1.5
1
0.5
0
-0.5
-1
-1.5
-2
-2.5
-3
-4
-3
-2
-1
0
1
2

Figure 3



Number of participants assigning central cluster items to categories
600
500
400
300
200
100
0
rapid
effort
concentration
not in
tight
running out of air
stops
exercise
disease
stress
other
unknown

# CHAPTER 4

## Cognitive Representation and Affective Connotation of Respiratory Sensations in Health, Aging and Disease

# Cognitive structure and affective connotations of respiratory sensations in health, aging, and disease

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## Abstract

Background: Dyspnea is a multifaceted sensation in somatic and psychological disorders and its associated verbal descriptors are regarded as important source of diagnostic information. Although the affective experience accompanying dyspnea has been explored in the past, little is known about the affective connotation of individual sensation descriptors. In addition, current instruments measuring dyspnea operate under the assumption that its structure is uniform across healthy and diseased populations.

Method: We used Multidimensional Scaling and cluster analysis in combination with Preference Mapping to explore ratings of 25 descriptors of respiratory sensations regarding frequency of experience, associated discomfort, and situational incidence by individuals who reported suffering from respiratory disease (*n*=74), as well as younger (*n*=58) and older (*n*=50) individuals reporting no respiratory disease.

Results: The cognitive structure of sensation report differed between groups of participants. While latent dimensions of dyspnea were relatively stable across groups, clusters were more variable, possibly reflecting distinct mechanisms of breathlessness in health, age, and disease. Furthermore, sensory experiences differed in affective evaluation. In all groups except for older individuals, different sensory dimensions of dyspnea contributed simultaneously to feelings of discomfort associated with types of respiratory sensations.

Conclusion: Because of differences in the cognitive structure and affective evaluation between groups, the comparability of sensation report by younger and older healthy samples with samples of respiratory disease patients may be limited.

Keywords: respiratory sensation, affective evaluation, respiratory disease, older population, dyspnea

Abbreviations:

Chronic Obstructive Pulmonary Disease = COPD

Multidimensional Scaling = MDS

## INTRODUCTION

Verbal report of respiratory sensations is a valuable source of diagnostic information (American Thoracic Society, 1999; Davenport, 2002, Scano, Stendardi, & Grazzini, 2005; Manning & Schwartzstein, 1995; 2001). The structure of self-report of dyspnea by healthy individuals and patient groups suffering from a range of somatic and psychological disorders has been explored extensively by analyzing the perceived similarity between verbal descriptors of respiratory sensations using cluster analysis, Multidimensional Scaling (MDS), or factor analysis (Elliott et al., 1991; Harver, Mahler, Schwartzstein, 2000; Mahler, Harver, & Lentine, 1996; Meuret et al., 2006; Simon et al., 1989; 1990; Perna et al., 2004; Petersen, Orth, & Ritz, 2008; von Leupoldt et al., 2007). In most of theses studies however, a structure with clusters of qualitatively different types of dyspnea was identified across all groups and group comparisons have been made using this general cluster structure. The actual structure of sensation report has rarely been compared between groups in one study, although it can be assumed that, the structure of the language of dyspnea differs between groups at least on higher levels of aggregation, because different pathophysiological conditions have been shown to be characterized by unique sets of qualitatively distinct sensations (Manning & Schwartzstein, 1995; Scano et al., 2005). Similarities in the structure of symptom report between groups of patients and healthy individuals may have been overestimated by interpreting low fusion levels in cluster analyses (Petersen et al., 2008). Given the lack of direct evidence for the comparability of the cognitive representation of dyspnea (as reflected in the use of verbal sensation-descriptors) across groups, we sought to study whether solutions vary when the same set of methods, Multidimensional Scaling (MDS) and cluster analysis, were applied to three groups of individuals, younger and older healthy individuals as well as those reporting respiratory diseases. We expected that the exact structure of the cognitive representation of dyspnea would vary across groups.

Besides the cognitive representation, the affective evaluation of respiratory sensations has received only little attention in the past. It has been shown that sensory and affective aspects of dyspnea contribute both to the report of experience of general feelings of dyspnea (von Leupoldt, Ambruzsova, Nordmeyer, Jeske, & Dahme, 2006; Wilson & Jones, 1991). However, little is known about the affective component of specific respiratory qualities. Dyspnea is defined as an *uncomfortable* awareness of the need to breathe (American Thoracic Society, 1999) and the affectively unpleasant nature of dyspnea has been emphasized recently in studies of exertion in interstitial lung disease (O'Donnell, Chau, & Webb, 1998) or functional imaging (Evans et al., 2002; Morelot-Pazini et al., 2007, Peiffer et al., 2001). This affective evaluation of dyspnea is clinically relevant, because it is the aspect of dyspnea that motivates behaviour such as avoiding stimuli or seeking help (Banzett, Dempsey, O'Donnell, & Wamboldt, 2000).

A similar distinction of affective and sensory dimensions has been made for pain. However, it has been demonstrated that although semantically sensory, emotional and motivational dimensions of pain can be distinguished, these dimensions are highly interrelated and that the sensory dimension of pain is not independent from its affective evaluation. Clark et al. (2001) concluded that "a score on a pain rating scale is not a pure measurement of the patients pain, but is heavily influenced in unknown ways by the patient's emotional and motivational state" (p. 38). In addition, qualitatively different sensory experiences of pain can differ in their affective evaluation (Clark, Janal, & Hoben, 2001). Similarities between dyspnea and pain have been discussed for some time (Banzett & Moosavi, 2001) and it has been shown that these two multidimensional constructs share a number of similarities regarding perceptual processes (von Leupoldt et al., 2006; Wilson & Jones, 1991). Therefore, we hypothesize that in dyspnea, respiratory sensations have an affective connotation and that different qualitaties of dyspnea would differ in affective evaluation. Furthermore, we expected that affective evaluation of individual sensations would vary between healthy individuals of different ages and patients, possibly reflecting variations in physiological mechanisms and psychological consequences of breathlessness in health, aging, and disease processes.

Our approach is different from prior research on the affective component of dyspnea with asthma patients (Kinsman, Luparello, O'Banion, & Spector, 1973) or other patient groups suffering from a broader range of cardio-respiratory disease (Skevington, Pilaar, Routh, & Macleod, 1997) in which the affective evaluation of dyspnea has been operationalized by measuring the affective state associated with dyspneic episodes or by including additional affect-related descriptors, rather than exploring the affective connotation of individual respiratory sensations directly. In contrast to the assumption of an affective dimension of dyspnea that would be distinct from sensory dimensions of dyspnea, we expected different sensory dimensions to contribute to the affective quality of dyspnea simultaneously. To test this assumption we embedded clusters of respiratory sensations within a dimensional framework of latent dimensions of dyspnea identified using MDS and explored the contribution of these latent sensory dimensions to the feeling of discomfort associated with dyspnea.

With respect to affective evaluation, respiratory sensations subsumed under dyspnea might differ from pain in that not all of them are necessarily experienced as unpleasant. While disease-related respiratory sensations may be perceived as unsettling, others may be linked to normal daily activities and therefore not perceived as threatening, at least for healthy individuals. The affective evaluation of dyspnea therefore will have a broader range than the affective evaluation of pain. Differences in this emotional connotation may be related to causes and consequences of dyspnea in different groups of healthy and diseased individuals. Such differences could reduce the comparability of sensation ratings between these populations.

To summarize, we expected that individuals with different experiential backgrounds regarding dyspnea vary in their cognitive representation and affective evaluation of specific respiratory sensations, which could reflect different mechanisms and consequences of dyspnea in health and disease. Moreover, we hypothesized that affective and sensory components of breathlessness are not separate, but that each sensory experience has an affective connotation. Multiple latent sensory dimensions of dyspnea identified by MDS would contribute simultaneously to the feeling of discomfort associated with breathlessness.

## METHOD

### Participants

182 Participants (124 women) were selected from a larger sample (*N*= 657) recruited at the university department and by internet. An initial analysis of the frequency and structure of sensations in those reporting no chronic respiratory complaints (*N*=582) will be subject of a separate report (Petersen, Morenings, von Leupoldt, & Ritz, submitted). The study has been approved by the review board of the German Research Society. Information on the study was given in written form and participation was anonymous. For the current analysis, three subgroups were formed with regard to age and disease state with 58 younger participants not reporting chronic respiratory complaints (20-30 years old, mean age=23.5 +/-2.3), N=50 older participants not reporting chronic respiratory complaints (45-89 years old, mean age=57.5 +/-10.3), and N=74 participants who reported having a respiratory complaints (range 20-45 years, mean age=28.2 +/-9.5). To control for potential effects of on respiratory sensation report, we excluded individuals who were overweight (Body Mass Index>25), reported being heavy smokers (>20 cigarettes/day), and/or were above average in physical activity, exercising three or more times a week.

## Instrument

We used a list of verbal descriptors of respiratory sensations adapted from a 19-item list composed by Simon and colleagues (1989) for which we had previously established a meaningful cluster structure (Petersen et al., 2008) that concurs with evidence from respiratory physiology. We added four items describing sensations of intense and effortful breathing and one item referring to conscious regulation of breathing (Table 1). Participants rated all items with regard to frequency of experience (0=*never*/4=*very often*) and discomfort they associated with each sensation (0=*very pleasant*/4=*very unpleasant*). Subsequently, they indicated in which situations they were most likely to experience each sensation: 1) *sports/exercise,* 2) *emotions/stress*, 3) *illness*, and 4*) other situations* (to be specified). Finally, information on demographic and health-related variables (including a question about prior diagnosis of respiratory disease) was obtained using an ad-hoc questionnaire.

## Data Analysis

We used the XLstat program (Addinsoft, New York) for all steps of our analysis. We created one two-dimensional configuration for each subgroup, displaying distances between the 25 items based on their similarities regarding the three situations using the Chi² metric in an ordinal MDS. To asses the fit of the MDS model, we used Kruskals Stress index (Kruskal & Wish, 1994). As a convention stress value of .20 can be regarded as poor fit index, a value of .10 as fair fit, .05 as good fit, and .025 as excellent fit. Stress decreases, when more dimensions are included within a model. Thus, model fit has to be interpreted not as absolute value, but in relation to the number of dimensions in a model. Cluster structure was analyzed using the hierarchical Average Linkage algorithm. MDS and cluster analysis have been developed as theories of perception and are rooted in the tradition of psychophysical research (e.g. Torgerson, 1958). They offer the advantage of exploring dimensions and types of dyspnea by including *multiple* aspects of dyspnea *simultaneously,* for instance to explore dyspnea experienced in different situations simultaneously in one analysis (Kruskal & Whish, 1994). Traditionally, because the perception of dyspnea is state dependent and can arise in response to a multitude of different mechanisms (Davenport, 2007), cluster analysis and MDS have been the preferred methods in most studies on the report of dyspnea (Elliott et al., 1991; Harver et al., 2000; Mahler et al., 1996; Petersen et al., 2008; Simon et al., 1989; 1990; von Leupoldt et al., 2007; 2006). The combination of MDS and cluster analysis in a joint-representation served as internal validation indicating to what degree these methods led to congruent findings (Everitt, 1974; Kruskal & Whish, 1994). Furthermore, such a combination of a dimensional approach can help to decide on the number of clusters to analyze (Everitt, 1974) and can support the understanding of group differences in cluster structures.

The initial orientation of MDS dimensions is arbitrary. Therefore, configurations cannot be interpreted and compared meaningfully without rotation (Peay, 1988). We used Generalized Procrustes Analysis to orthogonally rotate the three configurations to an optimal agreement (Gower, 1975). Procrustes Analysis can be used to generate one consensus matrix out of several configurations. However, we used the method only to reach optimal agreement between rotations and without changing the relative distances between descriptors.

**Preference Mapping**

Preference Mapping combines the analysis of perceived similarities between objects via MDS with the analysis of their affective evaluation (Chang & Carroll, 1989). Using this method, the variance explained by latent dimensions of dyspnea for discomfort associated with dyspnea or frequency ratings for dyspnea can be explored via regression analysis. While this method is common in economy and marketing research (Schenkman & Joensson, 2000) and has been used in research on pain (Clark et al., 2001), it has been largely disregarded in the analysis of respiratory symptom perception. We embedded two regression lines per map, here referred to as vectors, one for aggregated discomfort and one for frequency ratings for each group of individuals. Projections of descriptor points on these vectors were maximally related with frequency or discomfort ratings, respectively, i.e. discomfort and frequency increase in the direction their vector is pointing. The length of the vectors is determined by the multiple regression coefficient $R^2$ of the model. The better the model is adjusted, the longer is the corresponding vector. Beta-values of the regression coefficient can help to explore the contributions of the single dimensions of the perceptual space to discomfort and frequency ratings (see e.g. Schenkman & Joensson, 2000).

## RESULTS

### Clusters and dimensions of dyspnea

Two MDS dimensions, interpreted as *effort* and *fit between need for air and actual breathing* (here referred to as *fit*-dimension) were identified for healthy participants and participants with respiratory disease (Kruskals Stress 1=.094 younger healthy participants, .044 participants with respiratory disease) (Figure 1,3). The subgroup of older participants yielded one dimension also interpreted as fit-dimension, but the second dimension was not interpretable, because clusters of respiratory sensation descriptors showed only a clear differentiation on the first dimension and highly overlapping in their distribution on the second dimension (Kruskals Stress 1=.052) (Figure 2). Good joint representations were found for all groups, which can be regarded as an internal validation of these explorative results.

With cluster analysis we identified four largely but not completely comparable clusters in the three subgroups, which we interpreted as 1) *effort,* 2) *obstruction,* 3) *arrest of breathing,* and 4) *struggling for air* (Figures 1-3). In healthy, younger individuals, a subcluster of effort was found, interpreted as *problems with coordination of breathing*, which was embedded in the effort cluster and constituted by the items “not in”, “not out”, and “not enough” close to the items “concentration” and “air-hunger”. Compared to healthy younger participants, six items differed regarding their clusters assignment in the cluster solution for older participants and for participants with pulmonary disease (Table 1).

**Preference analysis**

Because cluster affiliations of items varied between groups, a quantitative comparison of clusters ratings using an ANOVA design was not reasonable. Using preference analysis, differences in frequency and discomfort rankings of descriptors between groups were found. For all three configurations a good model fit was obtained (Table 2). Participants with respiratory disease showed strongest associations of discomfort with descriptors of the cluster obstruction, healthy participants with the subcluster ‘problems with coordination of breathing’. Older participants were the only group that indicated the space around the descriptor ‘suffocation’ to be most uncomfortable. Differences were also found regarding frequency of respiratory sensations. In all three configurations, the item describing deep breathing was placed in the struggling for air cluster and associated with only little discomfort. However, while it was perceived as highly frequent for younger and older participants, it was ranked as least frequent of all struggling for air items in individuals suffering from respiratory disease.

Table 3 displays regression coefficients illustrating the association of the dimension effort and fit with frequency and discomfort ratings. For the healthy younger participants and participants who reported respiratory disease, both dimensions were related to the experience of discomfort. For older participants, only the fit-dimension explained discomfort, whereas the regression coefficient for the second dimension was close to zero. Please note that for this regression analysis not individual data was used, but descriptor coordinates on the two dimensions and discomfort and frequency ratings aggregated across groups. Rotation of configurations to another degree would have led to other regression coefficients, but not to comparable and interpretable dimensions. Thus, these results have value regarding the comparison of groups but should not be taken as absolute values.

## DISCUSSION

Our analysis revealed three comparable configurations that confirmed a previously observed dimensional structure of dyspnea (Petersen et al., 2008). These underlying dimensions were labelled ‘effort’ and ‘fit between need for air and actual breathing’, bearing similarity with findings in respiratory medicine that identified effort and obstruction as superordinated qualities of dyspnea (Banzett et al., 2000; Binks et al., 2002; Moy et al., 2000). A lack of fit between efferent motor command to respiratory muscles and afferent peripheral feedback as result of actual respiration has been assumed as one underlying mechanism of dyspnea (e.g. American Thoracic Society, 1999; Scano et al., 2005).

The similarities in the dimensional structure observed across subject groups may reflect a more global cognitive representation of dyspnea across health and disease. In contrast, the higher variation found in cluster structures within such a dimensional space could possibly show a higher sensitivity of cluster analysis for specific forms of dyspnea and their underlying physiological mechanisms in health and disease. Only in the healthy younger group, problems with coordination emerged as a subcluster as observed in prior experimental dyspnea induction in healthy younger individuals (Petersen et al., 2008). Compared to the younger group without reported respiratory disease, six items in the configuration of the older group shifted from the clusters struggling for air and obstruction into the effort cluster in the centre of the fit dimension which could be interpreted as a cluster with an ambiguous status regarding a benign or pathological character. Conversely, in individuals reporting respiratory disease, five descriptors shifted from struggling for air to effort and from effort to obstruction, indicating an overall shift towards a more disease-related connotation. These results confirm our hypothesis that the cognitive representation of dyspnea differs between groups of individuals with different experiential backgrounds regarding breathing and breathlessness. In contrast to prior practice, cluster structures should not be generalized across different groups. To evaluate the comparability of cluster structures found in different groups of individuals, the comparability of the location of clusters on latent dimensions of dyspnea should be analyzed.

Our results with Preference Mapping showed that groups of individuals also differed in the unpleasantness they attributed to particular groups of respiratory sensations. However, the location of the hypothetically most unpleasant point within the MDS configurations was very similar for younger healthy individuals and those reporting respiratory disease, characterized by low fit and high effort, occupied by the subcluster 'problems with coordination' for healthy younger subjects and 'obstruction' for those reporting respiratory disease. Sensations most problematic from a functional viewpoint, such as suffocation, were rated to be most discomforting only by older subjects. It could be speculated that this was due to the retrospective character of the study. If participants had been asked to rate discomfort directly after an adequate experimental stimulus, they might have been more likely to rate suffocation to be the worst. It could be assumed that the identified vectors did not represent *absolute discomfort* but *relevant discomfort*, pointing to the area of the configuration with the sensations most uncomfortable as well as most relevant for a particular group. Healthy younger individuals may only become aware of their breathing when coordinating breathing in and out becomes a problem and may rarely experience problems related to inspiration or expiration in isolation. In contrast, in respiratory diseases such as asthma, items related to airway obstruction are the most important respiratory sensations descriptors to characterize exacerbations (Banzett et al, 2000; Binks et al., 2002; Moy, Wodrow-Weiss, Sparrow, Israel, & Schwartzstein, 2000; O'Donnell et al., 2007). In general, comparing ratings of healthy controls and patient groups may be problematic due to the sometimes radically different experience base in health and disease. Furthermore, the connotation of a descriptor can change when it is combined with other descriptors, as can be seen in the cluster 'problems with coordination'. Each item of this cluster can constitute a type of dyspnea in its own, such as the item "My breath does not go in all the way" describing a form of obstruction. However, in combination with other items its meaning can change. Problems with coordinating breathing in and out constitute a quality of dyspnea that can be distinct from obstruction. Future research including healthy samples should strive to control for differences in connotations of sensations between healthy and diseased populations. Our findings also suggest that problems with coordination of breathing, especially coordination of breathing and speaking are an important source of dyspnea in healthy individuals as has been suggested for patients with respiratory disease (Skevington et al., 1997; Lee, Friesen, Lambert, & Loudon, 1998). This type of dyspnea should be addressed more directly in future studies.

In all groups except in older participants, both latent dimensions of dyspnea identified using MDS contributed simultaneously to feelings of discomfort associated with types of dyspnea. However, in older participants a clear differentiation on the fit-dimension was combined with a lack of differentiation on a second dimension. A reduced sensitivity for different qualities but not for the intensity of symptoms has been found before in older patients with pain, a sensation that is often interpreted as a normal consequence of aging and mostly ignored by older individuals (Gagliese & Melzack, 2003; Yong, Gibson, & Horne, 2001). Further research is needed to explore whether a possible lack of differentiation in sensation report in older individuals is due to a physiologically based insensitivity for different qualities and/or a growing stoicism towards bodily discomfort. Possible age-related problems in distinguishing qualities of dyspnea would be problematic for diagnostic practice and should be further investigated.

A number of limitations of our study should be noted. Preference-mapping is an explorative method that displays relative discomfort and frequency and does not allow for a quantitative comparison. However, because of differences between groups of individuals in descriptors assigned to clusters and differences in the affective connotation of descriptors, such a quantitative comparison would not be meaningful. Also, information on respiratory disease was only obtained by self report in our study. Nevertheless, some confidence may be gained from the high similarities between clusters and dimensions found in the present study and results of a prior study inducing dyspnea with respiratory challenge tests (Petersen et al., 2008). Because of the high prevalence of depression and anxiety in individuals suffering from pulmonary disease (Opolski & Wilson, 2005; Norwood, 2006), not controlling for negative affect may have influenced our results. However, it is not known whether this would exert a more general influence on the level of the reported sensations (Watson & Clark, 1884) or whether it would apply only to specific sensations, and the extent to which particular forms of psychopathology (e.g. panic disorder, depression) would have a specific influence on the cognitive structure and affective evaluation of respiratory sensations.

In conclusion, our results show that the cognitive representation and affective connotations of various aspects of dyspnea varies with health status and age, thus limiting the comparability of dyspnea constructs between populations. In clinical research with healthy control groups, the ambiguity of descriptors regarding their pathophysiological character should be reduced and the affective evaluation should be controlled to ensure comparability of findings between groups.

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*Table 1.* Assignment of respiratory sensation descriptors to clusters for the three participant-groups.

| Respiratory sensation descriptors | Younger healthy participants | Older healthy participants | Participants with pulmonary disease |
|---|---|---|---|
| I feel out of breath. | Struggling for air | Struggling for air | Struggling for air |
| I feel that I am breathing more. | Struggling for air | Struggling for air | Struggling for air |
| My breath goes deep into my lungs. | Struggling for air | Struggling for air | Struggling for air |
| My breathing is fierce. | Struggling for air | Struggling for air | Struggling for air |
| My chest heavily raises and lowers. | Struggling for air | Struggling for air | Struggling for air |
| I feel that my breathing is rapid. | Struggling for air | Struggling for air | Struggling for air |
| I am panting for more air. | Struggling for air | Effort | Effort |
| I am gasping for breath. | Struggling for air | Effort | Effort |
| My breathing requires more effort. | Effort | Effort | Effort |
| My breathing requires more work. | Effort | Effort | Effort |
| I feel a hunger for more air. | Effort | Effort | Effort |
| My breathing is heavy. | Effort | Effort | Effort |
| My breathing requires more concentration. | Effort | Effort | Effort |
| I cannot get enough air. | Effort /coordination | Effort | Obstruction |
| My breath does not go out all the way. | Effort /coordination | Effort | Obstruction |
| My breathing does not go in all the way. | Effort/coordination | Obstruction | Obstruction |
| I feel that I am smothering. | Obstruction | Effort | Obstruction |
| My chest feels tight. | Obstruction | Obstruction | Obstruction |
| I cannot take a deep breath. | Obstruction | Obstruction | Obstruction |
| My chest is constricted. | Obstruction | Obstruction | Obstruction |
| My breathing is shallow. | Obstruction | Obstruction | Obstruction |
| I regulate my breathing. | Arrest of breathing | Effort | Effort |
| I am running out of air. | Arrest of breathing | Effort | Arrest of breathing |
| I feel that my breath stops. | Arrest of breathing | Arrest of breathing | Arrest of breathing |

*Table.2*

Model fit indices for the Preference Mapping models of the three subgroups

| | *df* | $R^2$ | *F*-ratio | *p* |
|---|---|---|---|---|
| Younger healthy participants | | | | |
| Frequency | 2 | .493 | 10.68 | .001 |
| Discomfort | 2 | .479 | 10.13 | .001 |
| Older healthy participants | | | | |
| Frequency | 2 | .494 | 10.75 | .001 |
| Discomfort | 2 | .419 | 7.94 | .003 |
| Participants with pulmonary disease | | | | |
| Frequency | 2 | .282 | 4.33 | .026 |
| Discomfort | 2 | .587 | 15.64 | < .001 |

*Table 3*

| Discomfort | | | | | Frequency | | | |
|---|---|---|---|---|---|---|---|---|
| Younger individuals | *B* | *SE* | *t* | *p* | *B* | *SE* | *t* | *p* |
| fit | -.376 | *.013* | 29.463 | <.001 | 366 | 0.012 | 29.587 | <.001 |
| Effort | .423 | *0.026* | 16.226 | <.001 | -.463 | 0.025 | -18.319 | <.001 |
| pulmonary disease | *B* | *SE* | *t* | *p* | *B* | *SE* | *t* | *p* |
| fit | -.367 | .020 | 17.931 | <.001 | .476, | .017 | -27.734 | <.001 |
| Effort | .365 | .029 | 12.754 | <.001 | .087 | .024 | 3.605 | .002 |
| older individuals | *B* | *SE* | *t* | *p* | *B* | *SE* | *t* | *p* |
| fit | -.408 | .020 | 20.373 | <.001 | .401 | .018 | -22.381 | <.001 |
| Effort | .012 | .050 | -.247 | .807 | .188 | .045 | 4.184 | <.001 |

Figure legends

*Figure 1.* Joint representation of clusters embedded as ellipses in the MDS configuration for the group of younger participants without reported respiratory disease with frequency (dotted line) and discomfort regression lines.

*Figure 2.* Joint representation of clusters embedded as ellipses in the MDS configuration for the group of older participants without reported respiratory disease with frequency (dotted line) and discomfort regression lines.

*Figure 3.* Joint representation of clusters embedded as ellipses in the MDS configuration for the group of participants with reported respiratory disease with frequency (dotted line) and discomfort regression lines.

Figure 1

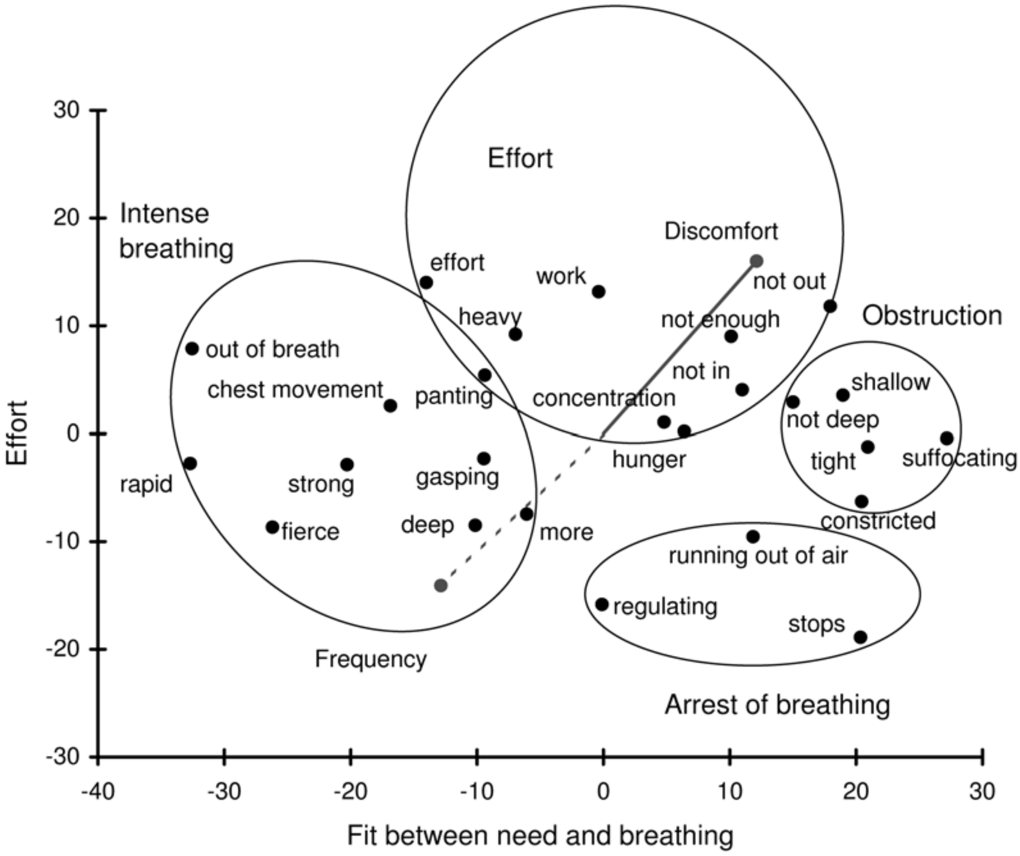
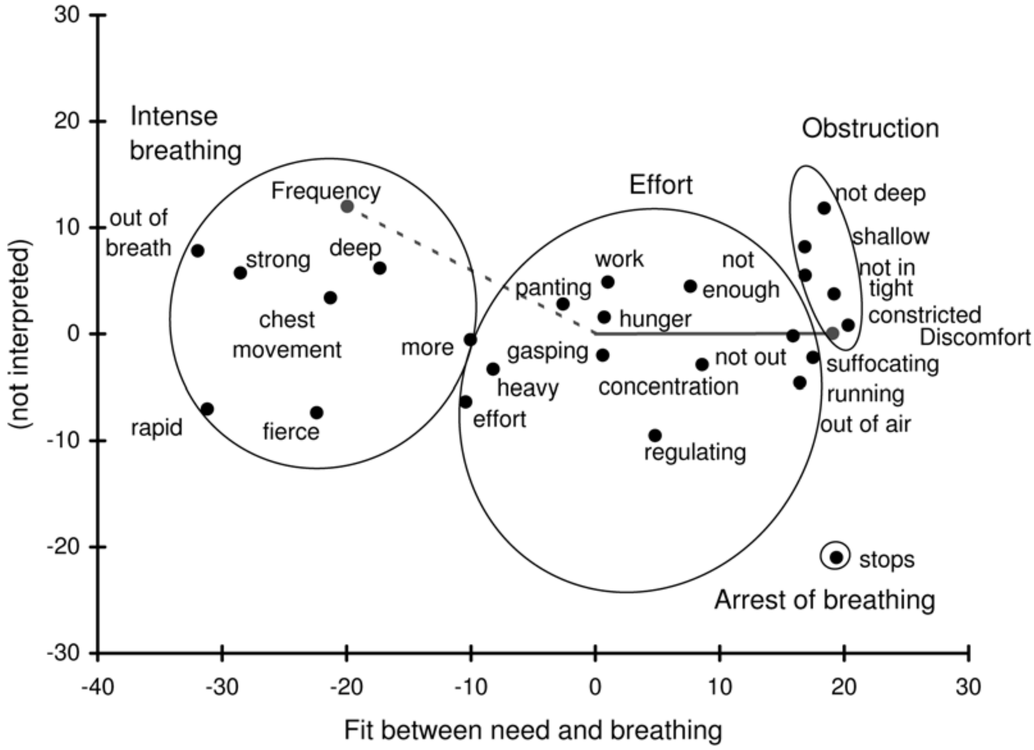
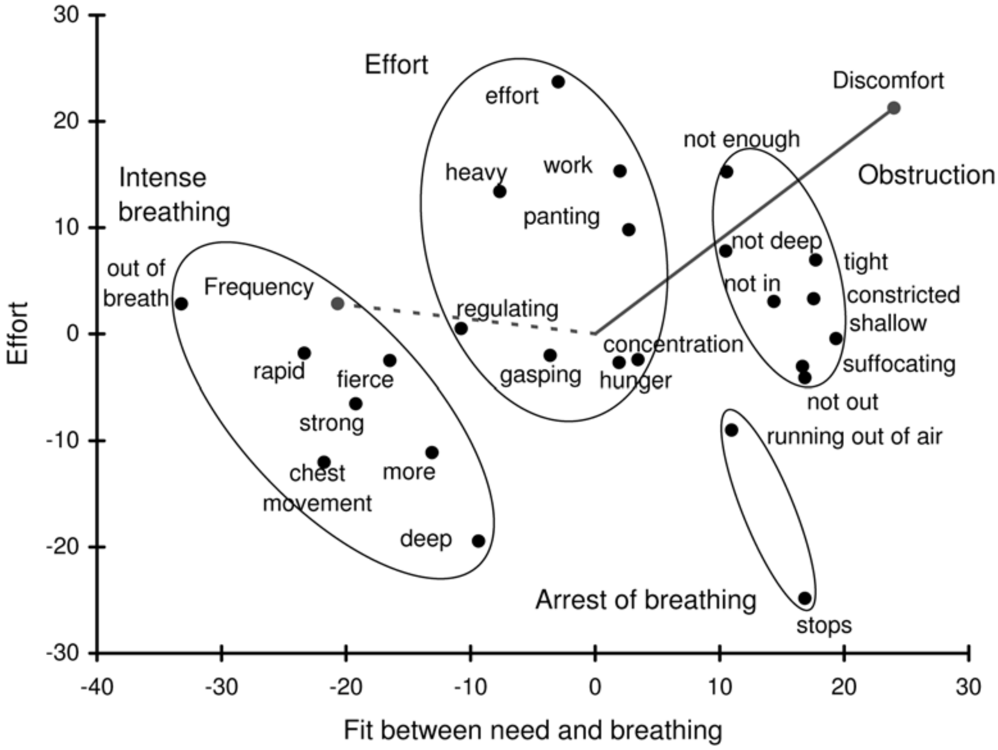

Effort
Intense breathing
Discomfort
Obstruction
Frequency
Arrest of breathing
effort
work
heavy
not out
not enough
out of breath
not in
chest movement
panting
concentration
shallow
not deep
hunger
rapid
strong
gasping
tight
suffocating
fierce
deep
more
constricted
running out of air
regulating
stops
Effort
Fit between need and breathing
30
20
10
0
-10
-20
-30
-40
-30
-20
-10
0
10
20
30

Figure 2



Intense breathing
Frequency
out of breath
strong
deep
chest movement
more
rapid
fierce
Effort
work
not enough
panting
hunger
gasping
heavy
effort
concentration
not out
regulating
Obstruction
not deep
shallow
not in
tight
constricted
Discomfort
suffocating
running out of air
stops
Arrest of breathing
(not interpreted)
Fit between need and breathing
30
20
10
0
-10
-20
-30
-40
-30
-20
-10
0
10
20
30

Figure 3


Effort
effort
Discomfort
not enough
heavy
work
Obstruction
Intense
breathing
panting
not deep
tight
out of
breath
Frequency
not in
constricted
regulating
shallow
concentration
rapid
fierce
gasping
hunger
suffocating
strong
not out
running out of air
chest
movement
more
deep
Arrest of breathing
stops
Fit between need and breathing
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# GENERAL DISCUSSION AND CONCLUSION

The report of respiratory sensations can provide useful information on underlying mechanisms of dyspnea. However, crucial for an evaluation of the validity of self-report in terms of its accuracy in reflecting changes in physiological states is an understanding of the structure and meaning of sensation report. Lavietes (2005) has criticized the use of lists of descriptors remarking that “it is not reasonable to expect all people, even if they speak the same language, to link the same word or descriptor to a given sensation“(p. 1877). Our results seem to confirm this criticism. As predicted in Hypothesis 1, we identified clusters of respiratory sensations and dimensions of dyspnea which were corresponding with respiratory challenges inducing qualitatively different breathing experiences (Chapter 1). However, cluster structures varied between studies and groups of individuals (Chapter 1-4), as well as within groups of individuals across repeated assessments (Chapter 2). Furthermore, we confirmed Hypothesis 2 and 3 by finding variations in the affective evaluation between sensations and variations in the cognitive and affective representation of dyspnea between groups of individuals with different experiential backgrounds regarding breathlessness (Chapter 3- 4). We found that not all respiratory sensations commonly subsumed under dyspnea (defined as an uncomfortable awareness of the need to breathe, American Thoracic Society, 1999) are necessarily perceived as uncomfortable by healthy individuals (Chapter 3). Furthermore, healthy and diseased individuals formed different rank orders when assessing the discomfort associated with different respiratory sensations (Chapter 4). Moreover, as predicted in Hypothesis 2 and 4 our results suggest that the affective and sensory components of breathlessness are not separate, but each sensory experience has an affective connotation (Chapter 3, Chapter 4), with different latent sensory dimensions of dyspnea contributing simultaneously to the feeling of discomfort associated with breathlessness (Chapter 4). Our results suggest that a comparison between groups on the basis of a general cluster structure derived across these groups, as it has been done in prior research (e.g. Elliott et al., 1991; Harver et al., 2000; Mahler et al., 1996), can be regarded to be problematic.

*The Cognitive Structure of Sensation Report*

Our results confirm doubts on the comparability of clusters of respiratory sensations found in different groups of individuals. However, our results also suggest possible ways to overcome these problems resulting from this lack of comparability for research and clinical practice. We found latent dimensions of dyspnea to be more stable across studies and groups of individuals with a different experiential background regarding dyspnea than cluster structures (Chapter 1-4). Furthermore, as we found in the study described in Chapter 4, the association of these latent dimensions with feelings of discomfort was comparable between younger healthy individuals and younger individuals suffering from respiratory disease. Thus, a dimensional approach in addition to traditional categorical approaches such as suggested by De Boeck et al. (2005) can be assumed to be helpful in assessing the comparability of dyspnea ratings between groups of individuals. Our results suggest that, in analogy to the categorical/ dimensional framework developed for the diagnosis of psychological disorders (De Boeck et al., 2005), manifest indicators of dyspnea (clusters of sensation descriptors) are related to latent categories such as the activation of specific physiological mechanisms by different experimental stimuli (Chapter 1 and 2), and that these manifest and latent categories can be described by latent dimensions underlying dyspnea found with MDS (Chapter 1-4). As we have outlined in Chapter 3 and 4, such latent dimensions might be less affected by individual differences in the interpretation and evaluation of specific sensations. Therefore, latent dimensions of dyspnea should receive more attention in future research.

*Control of breathing in health and disease: fundamental difference or methodological artefact?*

In individuals without known respiratory disease, we found a parsimonious three dimensional representation of dyspnea with the dimensions 1) fit between need for air and actual breathing, 2) effort, and 3) attempt of voluntary control being the most important latent dimensions of dyspnea in healthy individuals (Chapter 1 and 3). While the first two dimensions have also been found in individuals suffering from respiratory disease (Chapter 4), the latter (attempt of voluntary control) was more prominent in individuals not suffering from respiratory disease. However, these differences in dimensions and clusters reflecting voluntary control and awareness of breathing between groups of individuals have to be interpreted with care. These variations in self-report could be related to fundamental differences in the experience of dyspnea between groups of individuals, but they could also be a methodological artefact. Besides the dimension 'attempt of voluntary control', the cluster 'problems of coordination of breathing in and out' can serve as an illustration for this assumption of methodological shortcomings in the assessment of dyspnea. We found this cluster in the sensation-report of healthy individuals after experimental induction of dyspnea (Chapter 1), as well as in retrospective report (Chapter 3 and 4), but not in the sensation-report of individuals suffering from respiratory disease (Chapter 4). However, it cannot be concluded that problems of coordination that can be overcome by voluntary control of respiration are not relevant in the experience of breathlessness by individuals suffering from respiratory disease. These differences in the structure of sensation report between groups of individuals could also illustrate a methodological problem associated with using a list of a limited number of respiratory sensations instead of a free response format. If specific descriptors such as problems with coordination of breathing are missing on such a list, participants cannot report them in another way than by selecting a number of descriptors of sensations which in interplay come close to their experience, but should not be interpreted as distinct qualities of dyspnea. A person not suffering from respiratory disease might choose a number of descriptors for problems with breathing in and breathing out to describe problems of coordination without intending to refer to chest tightness. Problems of coordination could be assumed to arise in situations, where breathing has to be coordinated with speaking, especially under stress or during exercise. Only in individuals suffering from respiratory disease, the report of problems of either breathing in or of breathing out would guide a diagnosis correctly to either vocal cord disorder or asthma (Weinberger & Abu-Hasan, 2007). Coordination of breathing has been found to be a problem not only in healthy individuals, but also in individuals suffering from respiratory disease (Skevington et al., 1997; Lee, Friesen, Lambert, & Loudon, 1998). However, the relevance of these difficulties with coordination could have been underestimated in prior research, because only a few studies have included this sensation in symptom lists used to assess dyspnea. Problems coordinating breathing in and out, and coordinating breathing and speaking should be included in future research on the language of dyspnea and it should be specified that other descriptors refer only to e.g. problems of breathing in and breathing out occurring in isolation. In doing so, it could be assessed which role feelings of the loss of voluntary control of breathing play in patient groups and how much such a dimension contributes to discomfort associated with dyspnea. It could be assumed that changes in the evaluation of dyspnea in response to medication or rehabilitation exercise are partly related to an increase in the perceived control over specific sensations. This assumption has received empirical support. In patients suffering from COPD, rehabilitation exercise training led to changes in the affective evaluation of dyspnea that were not related to changes in ventilation (Carrieri-Kohlman et al., 1996). Including descriptors that are directly related to control and coordination of breathing would be necessary to clarify the role of voluntary control of breathing in patient groups and healthy individuals.

However, completeness of sensation lists may not be achievable. To be useful in research and diagnosis, such lists can only combine a limited number of sensations. While in a medical model of asthma symptoms only a small number of symptoms are regarded as standard asthma symptoms, such as cough, wheezing, tight chest, shortness of breath, and night-time cough, studies on lay perspectives on asthma have found that parents of children with asthma name up to 136 unique symptoms to describe asthma they observe in their children (Yoos, Kitzman, McMullen, Sidora-Arcoleo, & Anson, 2005). This illustrates how difficult it would be to create complete and unambiguous lists of sensations, especially when such lists should also include culture specific symptom descriptors (Han et al., 2005; 2008; Hardie, Janson, Gold, Carrieri-Kohlman, & Boushey, 2000). Therefore, in measuring dyspnea instruments and analytical methods are needed that help to uncover differences in connotation of descriptors between groups with different experiential backgrounds regarding breathing.

*Assessing comparability of sensation reports between groups of individuals: the integration of sensation categories within a dimensional framework of dyspnea*

Including a dimensional approach additional within the traditional categorical approach could help to assess the comparability of self-report of respiratory sensations between subject-groups. Sensation clusters should only be compared between groups of individuals, if these clusters are comparable regarding their location on latent dimensions found in all groups. Furthermore, it could be tested in a confirmatory approach whether a direct assessment of the characteristics of respiratory sensations on such dimensions would lead to similar configurations in healthy and diseased individuals, and whether these configurations would be comparable to perceptual maps found with explorative approaches used in the studies reported in Chapter 1-4. Also, it would be interesting to investigate the differentiation between respiratory sensations on different dimensions of dyspnea in asthma patients with a relatively accurate perception of asthma symptoms versus patients showing an over- or under-perception of such sensations. It could be speculated that poor symptom perception is partly related to an over generalization of sensations, i.e. a lack of differentiation between benign and pathophysiological sensations, as has been found in older individuals in the study reported in Chapter 4.

Characterizing the experience of dyspnea on a limited number of underlying dimensions of dyspnea alone could be an economical alternative for research on dyspnea. However, such an approach might suffer from individual differences in the interpretation of labels of dimension that have been described above. In studies reported here (Chapter 1-4), we changed the interpretation of one latent dimension from need for air/air hunger to fit between need for air and actual breathing. Although the location of sensation descriptors on this dimension was comparable between studies, this re-interpretation was done to clarify that this dimension was not only related to a need for air that is experienced in response to the activation of chemoreceptors in the brain stem (air hunger defined by Scano et al. 2005), or activation of other components of the respiratory system in isolation, but in response to a potential mismatch of afferent information from the respiratory system and efferent command to the respiratory muscles that can include the activation of one or more component of the respiratory system and can give rise to a distressing urge to breathe which is independent of muscular effort (O'Donnell et al., 2007; Mahler, 2006). Even though this can be regarded as a rather subtle refinement, it outlines possible differences in interpretation of latent dimensions of dyspnea.

*The Affective Evaluation of Respiratory Sensations*

Valence or affective evaluation can be seen as fundamental in perceptual judgments (Wundt, 1896). The affective component of dyspnea guides behavior such as avoiding (or approaching stimuli) or seeking help. We found that the affective evaluation of single sensations varied. Results presented in Chapter 3 and 4 showed that some sensations were perceived to be more negative than others and that groups of individuals varied in their evaluation of sensations. These results suggest that there is not only an affective evaluative dimension of breathlessness, a continuum ranging from physiological to affective qualities of breathlessness such as suggested by Skevington et al. (1997), but that each physiological sensation has its own affective connotation that can differ with the experiential background of the person perceiving it. Furthermore, regarding latent dimensions of dyspnea we found that at least in two of our three groups the dimensions, 1) fit between need for air and actual breathing, and 2) effort contributed simultaneously to the perception of discomfort associated with respiratory sensations (Chapter 4). These results are in line with our findings on the cognitive structure of dyspnea, which show that latent dimensions of dyspnea are less affected by individual differences in interpretation of single sensation descriptors. The affective evaluation of dimensions underlying dyspnea might be more comparable between groups than the evaluation of specific clusters of sensations.

Especially in understanding disease management strategies chosen by patients, learning more about the affective component of specific qualities of dyspnea is fundamental. Analyzing individual differences in the affective evaluation of symptoms, as for instance in patients suffering from asthma, could help to identify individuals that are at risk for under- or over-estimating the potential danger associated with specific sensations, resulting either in a delay of seeking help, or in an overuse of medication and avoidance of benign stimuli that increase ventilation (such as physical exercise). The avoidance of exercise due to the misinterpretation of enhanced ventilation as disease-related can lead into a vicious circle of avoidance and a decrease of physical fitness resulting in an earlier onset of breathlessness during exercise, resulting in more avoidance, accelerating further the decrease in physical fitness and increasing inactivity-related health risks (e.g. Folgering & von Herwaarden, 1994). Such misinterpretations can be overcome by a re-evaluation of exercise-related respiratory sensations, as has been shown in patients suffering from COPD (Carrieri-Kohlman et al., 1996). Here, exercise training reduced ratings for intensity of dyspnea and associated discomfort even when respiratory parameters did not change. Such a reframing of the negative interpretation of respiratory sensations as alarm signals into a positive interpretation as normal response of the respiratory system to stronger physical activity could help improve symptom perception and disease management in individuals with poor symptom perception. In doing so, therapy needs to target the whole cognitive-affective framework a patient has about breathlessness and not specific sensations or emotions in isolation.

*Conclusion*

Qualities of dyspnea constitute an important source of information for diagnosis and self-management of a disease. Information on these qualities can only be provided by the individual experiencing dyspnea. Interpreting self-report poses unique challenges, especially in the case of the language of dyspnea. Here, verbal report can be more ambiguous and dynamic in terms of connotations and actual meaning compared to symptom domains that are limited to disease or injury. It will also strongly depend on the situational context and on the experiential background of the person perceiving dyspnea. As reviewed in the introduction, the perception of respiratory sensations depends on the background status of the respiratory system, on external or internal cues leading attention away from respiration, learning processes, and affective states. The bias against self-report in assessing physiological states that can be observed in psychophysiological research (see e.g. Smith et al., 1995) may be in part our inability to understand the complex and dynamic nature of perceptual processes and language, and has little to do with the validity of self-report itself. We should give up the idea of a unique and static meaning of language descriptors and seek for methods and approaches that bring into the focus of attention the variations in interpretation and evaluation of sensations depending on situational factors and experiential background variables. These variations in the structure of self-report as well as in the evaluation of sensations can further our understanding of potential physiological mechanisms underlying dyspnea and on processes of coping with symptoms and adaptation to physiological processes.

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