

**Masterthesis Clinical Health Psychology
Utrecht University**

**The relation between medically unexplained
symptoms and susceptibility to anticipatory state
social anxiety (measured with the acoustic startle
reflex and STAI)**

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Abstract

Background and aim: subjects with medically unexplained symptoms (MUS) show greater startle responsiveness resulting from aversive physiological stimulation compared with subjects without MUS. It has been suggested that an enhanced degree of anxiety is responsible for this effect. Current study attempts to determine whether subjects with MUS (HMUS subjects) are more susceptible to anticipatory state social anxiety compared with subjects without MUS (LMUS subjects). **Methods:** subjects were fifteen female college students. The acoustic startle reflex (ASR), and a self-assessment with the STAI-state anxiety questionnaire, were used as measures of the degree of state social anxiety. The differentiation between HMUS and LMUS was achieved by means of SCL-90 mean scores. The social speech task was used to induce state social anxiety in subjects. **Results:** in contrast to what was to be expected, there is no significant difference between experimental conditions with regard to the ASR of HMUS and LMUS subjects. Furthermore, there is no significant difference regarding the STAI-state measurements of HMUS and LMUS subjects between experimental conditions. **Conclusion:** having medically unexplained symptoms did not lead to a higher susceptibility to anxiety within the research population. Due to the limited n , reservations are to be taken into account with regard to the generalisation of the results.

Key words: acoustic startle reflex, STAI, anxiety, fear-potentiated startle, medically unexplained symptoms.



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Introduction

Medically unexplained symptoms (MUS) are physical symptoms, such as pain and fatigue, which cannot be explained by a known physiological condition (Nimnuan, Rabe-Hesketh, Wessely & Hotopf, 2001). Many patients in primary healthcare suffer from MUS. For instance, a study of inpatient admissions in Denmark showed that nearly 20% of high users of healthcare had no definite physical disorder to account for their admissions (Nimnuan et al., 2001). Likewise, a survey of a Dutch outpatient medical clinic showed that 52% of new referrals remained medically unexplained (Nimnuan, Hotopf & Wessely, 2001).

Patients who suffer from MUS experience significant distress in daily functioning on physiological, psychological and social accounts (Fink, Rosendal & Olesen, 2005; Barsky & Borus, 1999). Furthermore, MUS have substantial economical implications. Patients with MUS are high rate healthcare consumers and undergo more frequently expensive medical examination (Aiarzaguena, Grandes, Salazar, Gaminde & Sánchez, 2008; Reid, Wessely, Crayford & Hotopf, 2002; Barsky, Ettner, Horsky & Bates, 2001).

MUS, negative affect and anxiety

Several personality characteristics are correlated with MUS, like neuroticism, trait anxiety and negative affect (Kemeny, 2009; Bailey & Henry, 2007; Chen & Drummond, 2008; Rosmalen, Neeleman, Gans & de Jonge, 2007; Koh, Kim, Kim, Park & Han, 2008; Löwe, Spitzer, Williams, Mussell, Schellberg & Kroenke, 2008; Portegijs, Jeuken, van der Horst, Kraan & Knottnerus, 1996). Furthermore, MUS co-occur with depression and anxiety (Arnold, et al., 2007; Henningsen, Zimmermann & Sattel, 2003; Hanel et al., 2009). In addition, Hanel et al. state that the majority of patients with mild forms of mental illness in primary care are often diagnosed with somatoform/functional disorders, although the latent psychological illness is not diagnosed (2009). In sum, it seems that MUS, certain personality characteristics and psychological illnesses as depression and anxiety are interrelated.

Hypervigilance may contribute to the interrelation between MUS and psychological illness (Janssen, 2002). Hypervigilance can be defined as an intensified form of paying attention to specific stimuli. Heightened vigilance to physiological functioning is related to enhanced anxiety and an increase in the intensity of experienced MUS (Janssen, 2002; Crombez, Eccleston, van den Broeck, Goubert & van Houdenhove, 2002; Posserud, Svedlund, Wallin & Simrén, 2009). Anxiety, in turn, may invoke heightened attention (hypervigilance) to bodily sensations and more intense reactions to these sensations (Conrod, 2006; Naliboff et al., 2008). Thus, it seems that anxiety affects the experience of MUS through hypervigilance (Jones, Swain & Harwood, 1996).



The above described studies are correlational. Much is to be learned about the causal influence of anxiety on experienced physical complaints. A recent study performed by Naliboff et al. provided some causal insight into how affective mechanisms may be responsible for an increased physiological response in subjects with the inflammatory bowel syndrome or IBS (2008)¹. Naliboff et al. demonstrated that patients with IBS show an enhanced startle reflex during a threatening situation; anticipation of aversive bowel stimulation (2008). They concluded that this increased acoustic startle reflex in IBS patients may have resulted from enhanced anxiety due to the threat of aversive stimulation to the bowel region (Naliboff et al., 2008). In contrast, this enhanced anxiety response was absent in the healthy control group.

From theory to empirical investigation

Theoretically, it seems that MUS and anxiety are interrelated (e.g. Hanel et al. 2009; Naliboff et al., 2008). In addition, Naliboff et al., uncovered an enhanced anxiety response in IBS patients (2008). Current study goes further by examining whether subjects with and without MUS differ in susceptibility to anxiety. Susceptibility to anxiety is defined by how easily anxiety is induced in subjects. Under normal circumstances, anxiety induction is achieved more easily in subjects with a greater susceptibility to anxiety (Grillon, Duncko, Covington, Kopperman & Kling, 2007; Naliboff et al., 2008; Grillon, 2008; Conrod, 2006). Furthermore, to investigate the relation between MUS and susceptibility to anxiety, two MUS subgroups are formed based on the degree of reported MUS on the SCL-90 somatization subscale (Arrindell & Ettema, 1986). High scorers on the SCL-90 SOM scale were typed as high MUS (or HMUS) and low scorers as low MUS (LMUS).

State social anxiety induction and measurement

In general, anxiety induction is achieved by submitting an organism to an anxiety inducing condition. The induction of anxiety results in an enhanced state of anxiety with corresponding physiological effects (Grillon, 2008). In this study, the induction of an anxious state is achieved by means of a social stressor; the social speech task (appendix B). The subject is led to belief that (s)he has to perform a speech in front of behavioural experts. The anticipation of having to perform a speech in front of an audience induces (or enhances) anticipatory state social anxiety (e.g. Grillon et al., 2007; Gramer & Sprintschnik, 2008; Conrod, 2006; Phillips & Giancola, 2008). Furthermore, the induction of state social anxiety by means of the social speech task is achieved easily in laboratory settings. Thus, the social speech task is effective and useful for state social anxiety induction.

¹ IBS is a medically unexplained syndrome characterized by recurrent abdominal pain and discomfort combined with an altered bowel function (Naliboff et al., 2008).



The amount of state (social) anxiety is measured both through physiology (by means of the startle paradigm) and self-report (with the STAI-state; Spielberger, Gorsuch & Lushene, 1970). The advantage of assessing anxiety through physiology is that it is less influenced by intentional control compared with verbal reports like questionnaires (Grillon, 2008). Furthermore, subjects can be unaware of their anxious state (Tsunoda et al., 2008). However, the startle paradigm is able to accurately assess the degree of (unaware) experienced anxiety (Grillon, 2008; Blumenthal et al., 2005). It is stated that the higher the magnitude of the acoustic startle reflex (ASR), the greater the degree of induced or experienced anxiety (Naliboff et al., 2008).

Research question and hypotheses

The research question of main focus is: to which degree do medically unexplained symptoms affect the susceptibility to state social anxiety? To answer this research question, HMUS and LMUS subjects are subjected to the same type and level of state social anxiety induction, by means of the social speech task. The degree of anxiety is measured both through physiology and self-report, before and after anxiety induction. The following hypotheses have been formulated:

- *Hypothesis 1:* HMUS subjects show greater ASR potentiation after the induction of anxiety compared with LMUS subjects.
- *Hypothesis 2:* resulting from anxiety induction, the degree of reported state anxiety on the State-Trait Anxiety Inventory state subscale (STAI-state) will be greater for HMUS subjects compared with LMUS subjects.

Both hypotheses predict that HMUS subjects show greater susceptibility to state social anxiety compared with LMUS subjects. This is reflected in ASR enhancement and a greater degree of verbally reported state anxiety on the STAI-state.

Methods

Subjects

A sample of 16 female college students was selected on the degree of experienced MUS with the somatization subscale of the SCL-90 during pre-experimental subject selection (Arrindell & Ettema, 1986). The subjects' mean age in years was 20.23 ($SD = 2.05$). One subject was excluded from analysis due to contaminated data. The selected sample was homogenous with respect to age, sex and nationality. Based on mean scores on the



somatisation subscale of the SCL-90, respondents were classified into either high MUS (HMUS) or low MUS (LMUS). Cut-off criteria were defined as $.50 SD$ above (HMUS) and below (LMUS) the group mean².

Inclusion criteria for all subjects were no current use of psychoactive substances or medication, no known medical condition, no hearing deficits and the absence of personality disorders. These factors are known to influence the eye blink startle reflex and may jeopardize the reliability and validity of the obtained results. However, mild substances, like aspirin and ibuprofen, were tolerated. The presence of a medical condition, psychological disorders and medicine usage were enquired using general questions preceding the SCL-90 somatization subscale. No participants were excluded due to hearing deficits.

Instruments

Psychometric instruments

During the experiment, subjects filled out questionnaires about personal physiological functioning and state anxiety (appendix A)³. The SCL-90 somatization subscale assessed the degree of experienced MUS by subjects. The subscale consists of twelve items, each describing physiological complaints. Subjects indicated to which degree they experienced pain, fatigue, nervousness, dizziness, fear and panic attacks, anxiety, nausea and/or tension, on a five-point Likert scale (Arrindell & Ettema, 1986). A greater score on the SCL-90 somatization subscale reflected greater experienced MUS. The SCL-90 somatization subscale has high internal consistency ($\alpha = .86$). In addition, the SCL-90 overall reliability is high as well ($\alpha = .90$). Furthermore, the correlation (r) between SCL-90 subscales, as an indicator of construct validity, lies between $.40$ and $.70$ (Arrindell & Ettema, 1986). Thus, the SCL-90 was sufficient for assessing experienced physiological complaints.

The state subscale of the State-Trait Anxiety Inventory (STAI-state) assessed the degree of state anxiety. The STAI-state consists of 20 items assessing the subjects' mood state at the time of enquiry using a four-point Likert scale (van der Ploeg, 1982). Some items were recoded to make sure that a higher score on the STAI-state reflected a greater degree of state anxiety. The STAI-state enquiries about present tension, calmness, feelings of safety, confusion, rumination about stressful and negative events, fear, anxiety, indecision,

² Besides pre-experimental subject selection, the subjects also filled out the SCL-90 somatization subscale *during the experiment*. Once again, the subjects were divided in separate MUS subgroups, based on these SCL-90 scores. Consequently, the SCL-90 data obtained during subject selection was discarded.

³ The Liebowitz Social Anxiety Scale (LSAS) was also filled out during the experiment for assessing the amount of trait anxiety (Liebowitz, 1987). However, no analysis was performed on the obtained results. The LSAS is included in appendix A.



uncertainty and nervousness. The test-retest reliability coefficients (r) of the STAI-state subscale are .73 for men and .30 for women⁴.

Acoustic stimuli properties and data acquisition

The acoustic eye blink response (or ASR) was assessed with the Biopac MP150 system and recorded with AcqKnowledge 4.0 software (Biopac Systems Inc.). Electromyogram (EMG) activity of the orbicularis oculi was assessed with electrodes placed directly beneath the right eye. The first electrode was placed directly underneath the pupil of the right eye. The second electrode was placed lateral to the first with overlapping electrode patches. A third ground electrode measured the reference signal and was placed in the center of the forehead. The EMG signal was sampled at a rate of 2000 Hz.

The eye blink responses were elicited with acoustic startle stimuli, consisting of white noise with an intensity of 100 dB. The stimuli were presented binaurally through stereophonic headphones. The frequency of the startle stimuli ranged from 20 Hz to 20 kHz with a rise and fall time of less than one millisecond. The duration of a startle stimulus was 50 milliseconds. The mean interval between two stimuli was 20 seconds, alternating between 15 and 25 seconds to counteract learning effects (figure 1). Background noise was played throughout the session, with an intensity of 65 dB and a frequency ranging from 20 Hz to 20 kHz⁵.

Two acoustic startle tasks were delivered to each subject; a baseline startle task and an experimental startle task. Each task was preceded by four habituation trials of acoustic stimuli. These trials resembled the baseline and experimental trials and were used to induce the first habituation to the acoustic startle stimuli. Data on these trials were not used for data-analysis. After the habituation trials, two minutes of background noise was presented, after which the baseline- or the experimental task began. Each task consisted of eight trials. Figure one shows a schematic representation of the baseline startle task.

⁴ This low value for women is expected, because many situational factors influence state anxiety as opposed to trait anxiety. Accordingly, the test-retest reliability of the STAI-trait is higher; .84 for men and .88 for women (van der Ploeg, 1982).

⁵ The interested reader is referred to Blumenthal et al. (2005).



Figure 1. *The baseline trials. The downward arrows indicate startle stimuli. The numbers between the arrows indicate the passage of time (seconds) between startle stimuli.*

Social speech task

Between the startle tasks, subjects underwent anxiety induction by means of the social speech task. They were accused (hypothetically) from using their peers in order to gain academic success. In response to this accusation, the subject had to defend herself by preparing a plea. The subject was instructed that her plea would be taped and judged by behavioural experts on the degree of self-assurance and credibility shown by the subject (appendix B). The subject was given five minutes of preparation to come up with as many credible arguments as possible against the accusation. She was given a desk and a piece of paper on which she could write her arguments. Meanwhile, the experimenter placed a video camera in front of her on the desk to enhance the effectiveness of anxiety induction. The subject was notified when she had only two minutes left to come up with credible arguments. After four minutes of preparation she was notified that she had only one minute left.

This method of anxiety induction was used, because it has proven to be effective (e.g. Gramer & Sprintschnik, 2008). Furthermore, the topic of the plea, a hypothetical accusation made by peers, is a well-known problem faced by many students; subjects can relate to this accusation. Overall, the induction of state social anxiety by means of the social speech task is efficient and easily achieved.

Data preparation

Before statistical analysis on the data was possible, non-usable data was discarded. In doing so, one contaminated baseline trial was removed from analysis due to fluctuations in



baseline ASR measurements. The data of the remaining fifteen participants was converted in SPSS (version 15.0) for further statistical analysis (SPSS Inc.).

Eye blink EMG is a signal that oscillates in positive and negative directions around a zero-voltage level (Blumenthal et al., 2005). Because the negative and positive components of the waveform could cancel each other out in subsequent processing, the signal was rectified: the data points were converted in absolute values (Blumenthal et al, 2005). After rectification the signal was smoothed over ten data points to form a smooth eye blink response curve. The baseline values were determined at 20 milliseconds before the onset of the acoustic pulse. Eye blinks which occurred during 20 milliseconds after the presentation of the startle stimuli or which occurred 100 milliseconds after the presentation of the stimuli were discarded; they were too slow or too quick to be induced by the acoustic startle stimulus. The maximum response within 20-100 ms after the onset of the startle stimulus in microvolts (μV) and the area beneath the response graphs based on the smoothed data were computed and further analyzed using SPSS statistical package (SPSS Inc.). Furthermore, maximum response values were corrected for baseline per trial. For each subject, a mean maximum startle response was computed per dataset (i.e. for both startle tasks). The area of response was also corrected for baseline measures for each trial, after which a mean area was computed per dataset. Unlike the maximum response value, which only says something about the highest peak in the total response, the area of response gives information about the length and mean height of the response.

Experimental design

Current study used a mixed between/within-subjects design. The experimental conditions did not differ between subjects; all subjects underwent two startle tasks and anxiety induction by means of the social speech task between these startle tasks. Furthermore, each subject filled out the SCL-90 and the STAI-state questionnaires. In contrast, the degree of experienced MUS differed between subjects (HMUS and LMUS).

The dependent variable was the degree of experienced state social anxiety. The independent variable was the degree of experienced MUS. A greater change in the degree of reported/experienced state (social) anxiety between experimental conditions reflected greater susceptibility to state (social) anxiety. This change was measured both through physiology (ASR) and verbal reports (STAI-state).

Procedure

During the experiment, the subject was seated behind a desk. First, the subject read an information form about the supposed goal of the experiment. After the subject decided she wanted to participate, she signed an informed consent. Thereafter, the subject filled out a



booklet of questionnaires, consisting of the STAI-state and the SCL-90 somatization subscale (appendix A). When the subject was finished with filling out the questionnaires, she was escorted to another seat and placed about 1 meter in front of a poster. This poster depicted a calm natural scene. Subsequently, the electrodes were placed. Following subject preparation, the baseline startle task was administered (figure 1).

After the baseline trials, the subject was disconnected from the Biopac system (the electrodes remained on the face of the subject, but were disconnected from the system) and escorted back to her desk. At this point, the social speech task was introduced to the subject. The subject was given five minutes of preparation before her hypothetical plea would commence. After preparation, the subject again filled out the STAI-state anxiety questionnaire. Subsequently, she was escorted back to her seat in front of the poster, after which the experimental startle task was administered. She was told that directly after the experimental startle task she had to perform her plea in front of the video camera.

The experimental startle task marked the end of the experiment. The subject was debriefed about the true goal of the experiment. She was told that the anticipation of having to perform in front of a video camera was part of the experimental manipulation, in order to induce state social anxiety. The subject received her course credit after electrode removal.

Analysis

All statistical analysis were carried out with SPSS version 15.0 (SPSS Inc.). The Wilcoxon signed-ranks test was used to statistically analyze changes in the degree of experienced state social anxiety *within* the sample and *within* MUS subgroups. The Mann-Whitney *U* test was used to statistically examine changes in the degree of experienced state social anxiety *between* MUS subgroups⁶.

To statically analyze the degree of change in both ASR and STAI-state measurements between MUS subgroups, the baseline ASR/STAI-state measurements were subtracted from experimental ASR/STAI-state measurements. The outcome was used as an index for the degree of change in experienced state anxiety (ASR potentiation).

Results

Descriptives

The mean total STAI-state score of the sample before anxiety induction was 33.53 ($SD = 7.27$). The mean total STAI-state score of the sample after anxiety induction was higher;

⁶ The Mann-Whitney *U* Test is an excellent tool when working with small sample sizes and is preferred when working with data which is not normally distributed across the population, like physiological responses (e.g. Grimm, 1993).



40.07 ($SD = 11.54$). The mean total SCL-90 somatization subscale score of the sample was 17.07 ($SD = 6.29$)⁷. Further sample and subgroup characteristics are depicted in table one.

Table 1. *Sample characteristics; the mean scores on the STAI-state, SCL-90 SOM scale and mean age of the sample and the distinct MUS subgroups. The standard deviation (SD) is depicted between brackets.*

	Total [$n = 15$]	HMUS [$n = 4$]	LMUS [$n = 11$]
Age (years)	20.23 (2.05)	20.25 (1.89)	20.50 (2.07)
STAI-State pre	33.53 (7.27)	36.50 (12.07)	32.46 (5.05)
STAI-State post	40.07 (11.54)	43.75 (18.10)	38.73 (8.98)
SCL-90 SOM	17.07 (6.29)	25.50 (6.61)	14.00 (1.84)

Manipulation check

The Mann-Whitney U test was used to statistically analyze deviations in SCL-90 somatization scores *between* MUS subgroups. The SCL-90 scores differed significantly between MUS subgroups; $U = .00$; $p < .05$. To determine whether anxiety induction *within* the sample was successful, the Wilcoxon signed-ranks test was used (both for STAI- and ASR measurements). Analysis revealed that the rise in STAI-state scores between experimental conditions was significant; $Z = -3.21$; $p < .05$. Furthermore, the mean maximum ASR of the sample differed significantly between baseline and experimental ASR measurements; $Z = -2.04$, $p < .05$. In contrast, the mean area of the startle response did not differ significantly between baseline and experimental measurements; $Z = -1.04$, $p > .05$.

MUS, state anxiety and ASR potentiation

Analysis of ASR magnitude was composed of the distinct analysis of both the mean maximum ASR and the mean area of (the startle) response. Deviations in startle responses between experimental conditions were analyzed with the Wilcoxon signed-ranks test (*within subgroup analysis*) and the Mann-Whitney U test (*between subgroup analysis*).

Analysis revealed that the deviation in the mean maximum ASR measurements did not differ significantly *between subgroups*; $U = 11.00$; $p > .05$ (figure 2). However, statistical analysis *within the LMUS subgroup* revealed that the magnitude of the mean maximum ASR was significantly lower after anxiety induction; $Z = -2.40$; $p < .05$. In contrast, the mean maximum ASR *within the HMUS subgroup* did not differ significantly between measurements; $Z = -.06$; $p > .05$. Concordant with the results obtained from mean maximum

⁷ Subjects who scored above 17.07 during the experiment were labelled as HMUS. Four subjects were placed in this HMUS category. Eleven subjects scored below average and were labelled as LMUS.



ASR analysis, the mean area of response did also not differ significantly *between subgroups*; $U = 15.00$; $p > .05$ (figure 3). Although the LMUS subgroup graphically shows greater ASR potentiation on both experimental conditions (before and after anxiety induction), this difference was not significant; $U = 20.00$; $p > .05$ and $U = 18.00$; $p > .05$ respectively (figure 3; the standard deviation is added for emphasis).

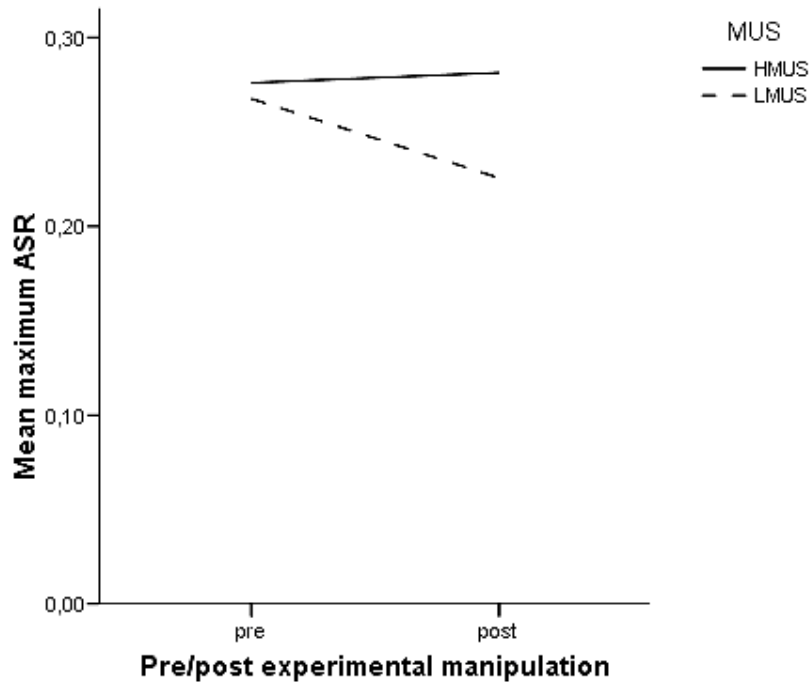


Figure 2. The mean maximum acoustic startle response (ASR) both before and after anxiety induction (pre and post experimental manipulation), depicted per MUS subgroup.

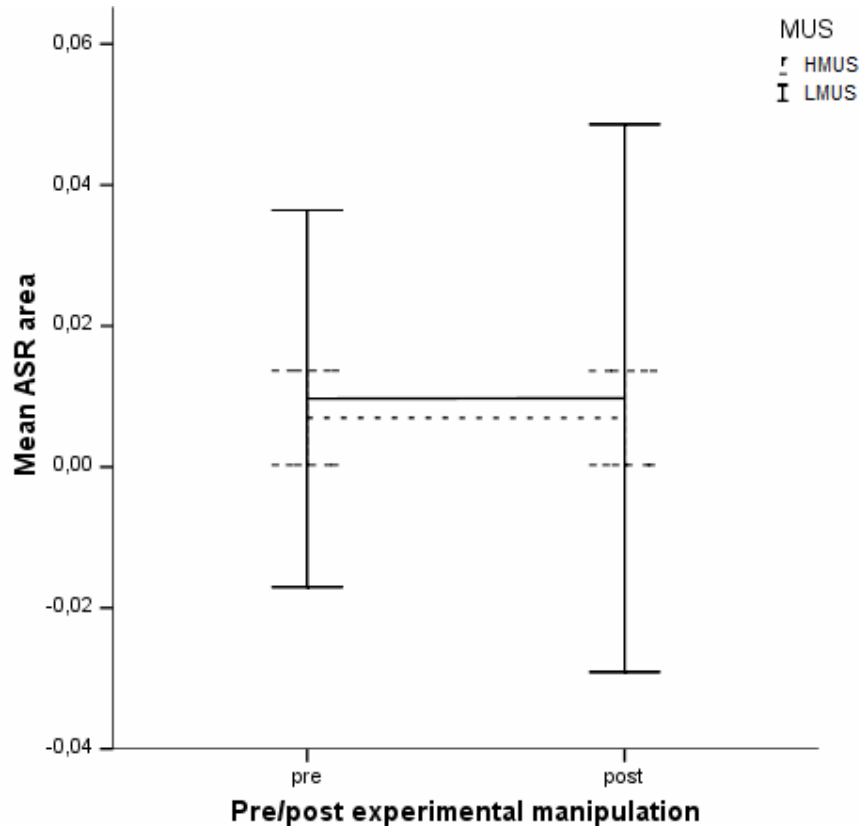


Figure 3. The mean area of the acoustic startle response (ASR) both before and after anxiety induction (pre and post experimental manipulation), depicted per MUS subgroup. The standard deviation is added for emphasis.

MUS and reported state anxiety

The Mann-Whitney U test was used to analyze *between subgroup* deviations in reported anxiety (STAI-state) between experimental conditions. Concordant with the ASR, the degree of reported state anxiety did not differ significantly between subgroups; $U = 21.00$; $p > .05$.

Discussion

The research question in current study is: to which degree do medically unexplained symptoms affect the susceptibility to state social anxiety? Results indicate that HMUS subjects do not show greater ASR potentiation compared with LMUS subjects. In addition, the degree of reported state anxiety on the STAI-state after anxiety induction is not greater for HMUS subjects compared with LMUS subjects. The results are discussed per hypothesis.



Hypothesis 1: MUS, state anxiety and ASR potentiation

Although the ASR magnitude does not differ significantly between subgroups, the mean maximum ASR of LMUS subjects reduces significantly after the induction of state social anxiety. In contrast, the ASR of HMUS subjects remain virtually unchanged after anxiety induction. These results contradict the stated hypothesis. Three possible explanations are offered, regarding 1) the type and effectiveness of the anxiety inducer, 2) the role of problematic habituation to aversive stimuli and 3) the effects of other uncontrolled variables.

The significant drop in mean maximum ASR measurements of LMUS subjects after anxiety induction may be an indicator that an inadequate anxiety inducer is used. Resulting from the use of an ineffective anxiety inducer, the degree of induced anxiety may be substantially lower than was intended. This, in turn, affects the degree of physiologically recorded anxiety by means of the ASR (e.g. Grillon, 2008). The fact that HMUS subjects do not seem to show this decline in startle reactivity may be because they are in fact more susceptible to anxiety compared with LMUS subjects.

Furthermore, the fact that the startle reactivity of HMUS subjects was not reduced, could be the result of problematic habituation (Behnke & Sawyer, 2004; Rief & Auer, 2001; Lim & Kim, 2005). Habituation can be defined as physiological recovery that occurs with repeated presentation of the same stimulus and that does not involve sensory adaptation/sensory fatigue or motor fatigue (Rief & Auer, 2001; Rankin et al., 2009). Generally, subjects with MUS show impaired habituation towards unpleasant stimuli (e.g. Coppola, Pierelli & Schoenen, 2009; Lowenstein et al., 2009; Andersson, Bende, Millqvist & Nordin, 2009). This may result from the fact that subjects with MUS are hypervigilant towards unpleasant or threatening stimuli, like acoustic startle stimuli and/or somatic complaints (Behnke & Sawyer, 2004; Rief & Auer, 2001; Lim & Kim, 2005; Naliboff et al., 2008).

Lastly, other uncontrolled variables than age, sex and nationality, could have influenced the obtained results. Studies suggest that other personality characteristics and types of psychopathology than anxiety may influence the experience of MUS. These are, amongst others, neuroticism, trait anxiety, negative affect and depression (Kemeny, 2009; Bailey & Henry, 2007; Chen & Drummond, 2008; Rosmalen et al., 2007; Koh et al., 2008; Löwe et al., 2008; Portegijs et al., 1996; Arnold et al., 2007; Henningsen et al., 2003; Hanel et al., 2009). However, the above described variables were not taken into account in this study.

Anxiety and diminished startle responsiveness

LMUS subjects seem to show a greater area of response (ASR) compared with HMUS subjects⁸. Interestingly, the empirical literature has documented a similar effect (e.g.

⁸ Since this effect is far from significant, it is most likely the result of chance.



Lang & McTeague, 2009). Lang et al. found that when subjects experience a profound state of anxiety, it could compromise the magnitude of the startle reflex (2009). Paradoxically, subjects with severe anxiety disorders, like panic disorder with agoraphobia, generalized anxiety disorder, or anxious subjects with comorbid depression, show a diminished startle response compared with subjects with less severe anxiety symptoms (Lang & McTeague, 2009). However, it is unlikely that this same effect has operated in current study, because none of the subjects suffered from severe anxiety disorders.

Hypothesis 2: MUS and reported state anxiety

HMUS subjects do not report a greater amount of state anxiety on the STAI compared with LMUS subjects after the induction of anxiety (van der Ploeg, 1982). However, it is known that verbal reports (e.g. of anxiety) can be influenced by intentional control (Grillon, 2008). Hence, it is possible that the amount of reported anxiety on the STAI-state does not correspond with the degree of actual experienced anxiety (e.g. Egloff & Schmukle, 2003). However, this pitfall is avoided by including physiological measures of anxiety, to objectively (i.e. outside conscious awareness) determine the degree of experienced anxiety (the ASR was used for this purpose). Because the degree of anxiety measured both through physiologically and self-report coincides, it is unlikely that the STAI-state measurements are inaccurate.

MUS and susceptibility to state social anxiety

Based on the data obtained in this study, there seems to be no relation between medically unexplained symptoms and susceptibility to anticipatory state social anxiety. Although anxiety and MUS often co-occur and share mutual influence (e.g. Hanel et al., 2009; Chen & Drummond, 2008; Löwe et al., 2008; Portegijs et al., 1996), the effects of MUS on the susceptibility to anxiety yet remain elusive. Needless to say, more research is required in order to counteract the individual and economical implications of MUS on society at large (e.g. Nimnuan et al., 2001; Fink et al., 2005; Barsky & Borus, 1999; Aiarzaguena et al., 2008; Reid et al., 2002; Barsky et al., 2001).

Future research

Due to the small sample size (see limitations), the conclusions made in this study are not powerful. Therefore, it can be argued that different and more valid results can be obtained when using a greater and more diverse sample size to enhance the power and validity of this study. Furthermore, by using subjects with a higher degree of MUS (e.g. clinical range), different results may be obtained.

In addition, the same experiment can be conducted but with more adequate anxiety inducing techniques. It is possible to physically induce anxiety with the finger press. This and



other physical techniques may be more relevant for subjects suffering from MUS, because both share a physiological component. As a result, the finger press may enhance the cognitive salience of MUS and elicit or enhance corresponding anxiety⁹. However, the possible surplus value of physical anxiety inducing techniques (e.g. the finger press) over psychological anxiety inducing techniques (e.g. the social speech task) has yet to be determined empirically.

Lastly, more research regarding the role of problematic habituation towards unpleasant stimuli must be conducted. The results obtained points in the direction of possible problematic habituation for subjects with MUS, towards unpleasant stimuli. Other studies also illustrate a relationship between problematic habituation to unpleasant or threatening stimuli and medically unexplained symptoms (e.g. Rief & Auer, 2001; Behnke & Sawyer, 2004). However, it is not yet clear what is responsible for this effect.

Limitations

Current study harbours several limitations. First of all, the small sample size is detrimental to the power of this study. With a sample size of 15 subjects and a medium effect size ($r = .05$), the mean overall power is .19, which is low. This increases the probability of making a type II error, or failing to reject the null hypothesis when it is in fact not true. Thus, it is possible that there was a treatment effect, but it was simply not detected. In addition, the difference in group size between both MUS subgroups is large. The sample is composed of four HMUS subjects and eleven LMUS subjects. Furthermore, the external validity of this study is low. The sample consists of Dutch female adolescent students. And lastly, the sample was divided in HMUS and LMUS based on an arbitrarily picked SCL-90 mean score. Overall, these factors jeopardize the credibility of the obtained results.

Conclusion

This study, with regard to its limitations, shows no difference between subjects with or without MUS on their susceptibility to state social anxiety. The induction of state social anxiety by means of the social speech task has a similar effect on subjects with as without MUS. HMUS subjects, compared with LMUS subjects, do not show a greater ASR potentiation resulting from anxiety induction. In addition, HMUS subjects do not report a greater amount of state anxiety on the STAI-state.

⁹ It is likely that the finger press activates existing cognitive schemata, formed by learning mechanisms and early life experiences. Amongst others, these schemata consist of information about MUS and accompanying bodily sensations. When one of these schemata is activated all become more salient and more easily activated. For example, the finger press may activate the schema 'MUS' by means of similar physiological properties (e.g. pain), therefore resulting in an increase in bodily sensations. These bodily sensations, in turn, may elicit anxiety (ten Broeke, van der Heiden, Meijer & Hamelink, 2008).



References

- Aiarzaguena, J.M., Grandes, G., Salazar, A., Gaminde, I. & Sánchez, Á. (2008). The diagnostic challenges presented by patients with MUS in general practice. *Scandinavian Journal of Primary Health Care*, 26, 99-105.
- Andersson, L., Bende, M., Millqvist, E. & Nordin, S. (2009). Attention bias and sensitization in chemical sensitivity. *Journal of Psychosomatic Research*, 66, 407-416.
- Arnold, I., Waal, M. de, Eekhof, J., Spinhoven, P., Assendelft, P. & Hemert, A. van (2007). Onverklaarde lichamelijke klachten en de samenhang met depressie en angst. *Huisarts & Wetenschap*, 50, 686-689.
- Arrindell, W.A. & Ettema, J.H.M. (1986). *SCL-90: handleiding bij een multidimensionele psychopathologie-indicator*. Lisse: Swets, Test Publishers.
- Bailey, P.B. & Henry, J.D. (2007). Alexithymia, somatization and negative affect in a community sample. *Psychiatry Research*, 150, 13–20.
- Barsky, A.J. & Borus, J.F. (1999). Functional somatic symptoms. *Annals of Internal Medicine*, 130, 910-921.
- Barsky, A.J., Ettner, S.L., Horsky, J. & Bates, D.W. (2001). Resource utilization of patients with hypochondriacal health anxiety and somatization. *Medical Care*, 39, 705-715.
- Behnke, R.R. & Sawyer, C.R. (2004). Public speaking anxiety as a function of sensitization and habituation processes. *Communication Education*, 53, 164-173.
- Blumenthal, T.D., Cuthbert, B.N., Filion, D.L., Hackley, S., Lipp, O.V. & Boxtel, A. van (2005). Committee report: guidelines for human startle eyeblink electromyographic studies. *Psychophysiology*, 42, 1-15.
- Broeke, E. ten, Heiden, C. van der, Meijer, S., Hamelink, H. (2008). *Cognitieve therapie: de basisvaardigheden*. Amsterdam: Boom.



- Chen, V. & Drummond, P.D. (2008). Fear of negative evaluation augments negative affect and somatic symptoms in social-evaluative situations. *Cognition and Emotion, 22*, 21-43.
- Conrod, P.J. (2006). The role of anxiety sensitivity in subjective and physiological responses to social and physical stressors. *Cognitive Behaviour Therapy, 35*, 216-225.
- Coppola, G., Pierelli, F. & Schoenen, J. (2009). Habituation and migraine. *Neurobiology of Learning and Memory, 92*, 249-259.
- Crombez, G., Eccleston, C., Broeck, A. van den, Goubert, L. & Houdenhove, B. van (2002). Hypervigilance to pain in fibromyalgia: the mediating role of pain intensity and catastrophic thinking about pain. *Clinical Journal of Pain, 20*, 98-102.
- Egloff, B. & Schmukle, S.C. (2003). Does social desirability moderate the relationship between implicit and explicit anxiety measures? *Personality and Individual Differences, 35*, 1697–1706.
- Fink, P., Rosendal, M. & Olesen, F. (2005). Classification of somatization and functional somatic symptoms in primary care. *Australian and New Zealand Journal of Psychiatry, 39*, 772–781.
- Gramer, M. & Sprintschnik, E. (2008). Social anxiety and cardiovascular responses to an evaluative speaking task: the role of stressor anticipation. *Personality and Individual Differences, 44*, 371-381.
- Grillon, C. (2008). Models and mechanisms of anxiety: evidence from startle studies. *Psychopharmacology, 199*, 421-437.
- Grillon, C., Duncko, R., Covington, M.F., Kopperman, L. & Kling, M.A. (2007). Acute stress potentiates anxiety in humans. *Biological Psychiatry, 62*, 1183-1186.
- Grimm, L.G. (1993). *Statistical Applications for the Behavioral Sciences*. Hoboken: John Wiley & Sons.



- Hanel, G., Henningsen, P., Herzog, W., Sauer, N., Schaefer, R., Szecsenyi, J. & Löwe, B. (2009). Depression, anxiety, and somatoform disorders: vague or distinct categories in primary care? Results from a large cross-sectional study. *Journal of Psychosomatic Research, 67*, 189-197.
- Henningsen, P., Zimmermann, T. & Sattel, H. (2003). Medically unexplained physical symptoms, anxiety, and depression: a meta-analytic review. *Psychosomatic Medicine, 65*, 528-533.
- Janssen, S.A. (2002). Negative affect and sensitization to pain. *Scandinavian Journal of Psychology, 43*, 131–137.
- Jones, G., Swain, A. & Harwood, C. (1996). Positive and negative affect as predictors of competitive anxiety. *Personality and Individual Differences, 20*, 109-114.
- Kemeny, M.E. (2009). Psychobiological responses to social threat: evolution of a psychological model in psychoneuroimmunology. *Brain, Behavior, and Immunity, 23*, 1-9.
- Koh, K.B., Kim, D.K., Kim, S.Y., Park, J.K. & Han, M. (2008). The relation between anger management style, mood and somatic symptoms in anxiety disorders and somatoform disorders. *Psychiatry Research, 160*, 372–379.
- Lang, P.J. & McTeague, L.M. (2009). The anxiety disorder spectrum: fear imagery, physiological reactivity, and differential diagnosis. *Anxiety, Stress and Coping, 22*, 5-25.
- Liebowitz, M.R. (1987). Social phobia. *Modern Problems of Pharmacopsychiatry, 22*, 141-173.
- Lim, S.L. & Kim, J.H. (2005). Cognitive processing of emotional information in depression, panic, and somatoform disorder. *Journal of Abnormal Psychology, 114*, 50-61.
- Löwe, B., Spitzer, R.L., Williams, J.B.W., Mussell, M., Schellberg, D. & Kroenke, K. (2008). Depression, anxiety and somatization in primary care: syndrome overlap and functional impairment. *General Hospital Psychiatry, 30*, 191-199



- Lowenstein, L., Kenton, K., Mueller, E.R., Brubaker, L., Heneghan, M., Senka, J. FitzGerald, M.P. (2009). Patients with painful bladder syndrome have altered response to thermal stimuli and catastrophic reaction to painful experiences. *Neurourology and Urodynamics*, 28, 400-404.
- Naliboff, B. D., Waters, A.M., Labus, J.S., Kilpatrick, L., Craske, M.G., Chang, L., Negoro, H., Ibrahimovic, H., Mayer, E.A. & Ornitz, E. (2008). Increased acoustic startle responses in IBS patients during abdominal and nonabdominal threat. *Psychosomatic Medicine*, 70, 920–927.
- Nimnuan, C., Hotopf, M. & Wessely, S. (2001). Medically unexplained symptoms: an epidemiological study in seven specialities. *Journal of Psychosomatic Research*, 51, 361-367.
- Nimnuan, C., Rabe-Hesketh, S., Wessely, S. & Hotopf, M. (2001). How many functional somatic symptoms? *Journal of Psychosomatic Research*, 51, 549-557.
- Phillips, J.P. & Giancola, P.R. (2008). Experimentally induced anxiety attenuates alcohol-related aggression in men. *Experimental and Clinical Psychopharmacology*, 16, 43-56.
- Ploeg, H.M. van der (1982). De Zelf-Beoordelings Vragenlijst (STAI-DY): de ontwikkeling en validatie van een Nederlandstalige vragenlijst voor het meten van angst. *Tijdschrift voor psychiatrie*, 24, 576-588.
- Portegijs, P.J.M., Jeuken, F.M.H., Horst, F.G. van der, Kraan, H.F. & Knottnerus, J.A. (1996). A troubled youth: relations with somatization, depression and anxiety in adulthood. *Family Practice*, 13, 1-11.
- Posserud, I., Svedlund, J., Wallin, J. & Simrén, M. (2009). Hypervigilance in irritable bowel syndrome compared with organic gastrointestinal disease. *Journal of Psychosomatic Research*, 66, 399–405.



- Rankin, C.H., Abrams, T., Barry, R.J., Bhatnagar, S., Clayton, D.F., Colombo, J., Coppola, G., Geyer, M.A., Glanzman, D.L., Marsland, S., McSweeney, F.K., Wilson, D.A., Wu, C.-F. & Thompson, R.F. (2009). Habituation revisited: an updated and revised description of the behavioral characteristics of habituation. *Neurobiology of Learning and Memory*, *92*, 135-138.
- Rief, W. & Auer, C. (2001). Is somatization a habituation disorder? Physiological reactivity in somatization syndrome. *Psychiatry Research*, *101*, 63-74.
- Reid, S., Wessely, S., Crayford, T. & Hotopf, M. (2002). Frequent attenders with MUS: service use and costs in secondary care. *British Journal of Psychiatry*, *180*, 248-253.
- Rosmalen, J.G.M., Neeleman, J., Gans, R.O.B. & Jonge, P. de (2007). The association between neuroticism and self-reported common somatic symptoms in a population cohort. *Journal of Psychosomatic Research*, *62*, 305–311.
- Spielberger, C. D., Gorsuch, R.L. & Lushene, R.E. (1970). *Manual for the State-Trait Anxiety Inventory*. Palo Alto, CA: Consulting Psychologists Press.
- Tsunoda, T., Yoshino, A., Furusawa, T., Miyazaki, M., Takahashi, Y. & Nomura, S. (2008). Social anxiety predicts unconsciously provoked emotional responses to facial expression. *Physiology & Behavior*, *93*, 172-176.



Appendix A

The questionnaires used during the experiment, consisting of the Symptom Checklist-90 somatization subscale (SCL-90), the Liebowitz Social Anxiety Scale (LSAS) and the State-Trait Anxiety Inventory state subscale (STAI-state). The STAI-state was filled out before the induction of state social anxiety and after to uncover changes in state anxiety due to the induction of anxiety.



Vragenlijst
SCL-90

Instructie

In onderstaande vragenlijst wordt je gevraagd in welke mate je last hebt van lichamelijke en psychische klachten. Geef voor elk van de onderstaande klachten aan in hoeverre je last hebt gehad, door een cirkel te plaatsen rondom het antwoord dat het meest van toepassing is.

Het gaat er hierbij om hoe je je **de afgelopen week, met vandaag erbij**, hebt gevoeld.

In welke mate word je gehinderd door:	helemaal niet	een beetje	nogal	tamelijk veel	heel erg
1. Hoofdpijn	1	2	3	4	5
2. Duizeligheid	1	2	3	4	5
3. Pijn in de borst of hartstreek	1	2	3	4	5
4. Pijn onder in de rug	1	2	3	4	5
5. Misselijkheid of een maag die van streek is	1	2	3	4	5
6. Pijnlijke spieren	1	2	3	4	5
7. Moeilijk adem kunnen krijgen	1	2	3	4	5
8. Je soms warm, dan weer erg koud voelen	1	2	3	4	5
9. Een verdoofd of tintelend gevoel ergens in je lichaam	1	2	3	4	5
10. Een brok in je keel	1	2	3	4	5
11. Je lichamenlijk ergens slap voelen	1	2	3	4	5
12. Zwaar voelen in armen of benen	1	2	3	4	5

Ga verder op de volgende pagina



Vragenlijst LSAS

Instructie

Hieronder volgen enkele vragen met betrekking tot sociale handelingen. Het is de bedoeling dat je aangeeft in hoeverre je bij de omschreven sociale handeling angst ervaart en in hoeverre je de handeling vermijdt. De waarden onder 'angst' geven aan hoeveel angst je ervaart bij de gegeven situatie. Je geeft de mate van angst aan door een cijfer te geven aan de situatie, waarbij het cijfer '0' voor helemaal geen angst staat en het cijfer "3" voor ernstige angst. Onder vermijding geef je een schatting in procenten van het totale aantal situaties die je vermijdt. Dit kan variëren van nooit (0; 0%) tot meestal (3; 67-100%).

Denk bijvoorbeeld aan de situatie van het geven van een presentatie. Wanneer dit veel angst in je oproept vul je het getal '3' in. Als het geven van een presentatie helemaal geen angst in je oproept, vul je '0' in. Wanneer je het geven van een presentatie meestal of altijd vermijdt, dus in 67% tot 100% van de situaties, vul je '3' in. Als je de situatie nooit vermijdt, dan vul je een '0' in.

Hieronder zie je de waarden die je kunt invullen:

Onder Angst:

- 0 = Geen
- 1 = Mild
- 2 = Gemiddeld
- 3 = Ernstig

Onder Vermijding:

- 0 = Nooit (0%)
- 1 = Soms (1—33%)
- 2 = Vaak (33—67%)
- 3 = Meestal tot altijd (67—100%)

Zie volgende pagina



Vragenlijst
LSAS

Onder Angst:

- 0 = Geen
- 1 = Mild
- 2 = Gemiddeld
- 3 = Ernstig

Onder Vermijding:

- 0 = Nooit (0%)
- 1 = Soms (1—33%)
- 2 = Vaak (33—67%)
- 3 = Meestal tot altijd (67—100%)

	Vrees of angst	Vermijding
1. Publiekelijk telefoneren		
2. Deelnemen aan kleine groepen		
3. In publieke plaatsen eten		
4. Met anderen wat drinken in publieke plaatsen		
5. Praten met mensen die autoriteit hebben		
6. Acteren, een voorstelling geven of praten tegenover een menigte		
7. Naar een feestje gaan		
8. Werken terwijl je geobserveerd wordt		
9. Schrijven terwijl je geobserveerd wordt		
10. Iemand bellen die je niet goed kent		
11. Praten met mensen die je niet goed kent		
12. Vreemden ontmoeten		
13. Plassen in een publiekelijk toilet		
14. Een kamer binnenkomen, wanneer de anderen al zitten		
15. In het middelpunt van de aandacht staan		
16. Je hoorbaar maken tijdens een vergadering		
17. Een toets maken		
18. Het uiten van afkeur naar mensen die je niet goed kent		
19. Mensen die je niet goed kent in de ogen kijken		
20. Een rapportage uitbrengen voor een groep		
21. Iemand proberen te versieren		
22. Goederen naar de winkel terugbrengen		
23. Een feestje geven		
24. Het weerstaan van een opdringerige verkoper		

Ga verder op de volgende pagina



Vragenlijst
STAI-state

Instructie

Hieronder vindt je een aantal uitspraken die mensen hebben gebruikt om zichzelf te beschrijven. Lees iedere uitspraak door en zet dan een kringetje om het cijfer rechts van die uitspraak om daarmee aan te geven hoe je je **nu voelt**, dus **nu op dit moment**. Er zijn geen goede of slechte antwoorden. Denk niet te lang na en geef jouw eerste indruk, die is meestal de beste. Het gaat er dus om dat je weergeeft wat je **op dit moment** voelt.

	geheel niet	een beetje	tamelijk veel	zeer veel
1. Ik voel me kalm	1	2	3	4
2. Ik voel me veilig	1	2	3	4
3. Ik ben gespannen	1	2	3	4
4. Ik voel me onrustig	1	2	3	4
5. Ik voel me op mijn gemak	1	2	3	4
6. Ik ben in de war	1	2	3	4
7. Ik pieker over nare dingen die kunnen gebeuren	1	2	3	4
8. Ik voel me voldaan	1	2	3	4
9. Ik ben bang	1	2	3	4
10. Ik voel me aangenaam	1	2	3	4
11. Ik voel me zeker	1	2	3	4
12. Ik voel me nerveus	1	2	3	4
13. Ik ben zenuwachtig	1	2	3	4
14. Ik ben besluiteloos	1	2	3	4
15. Ik ben ontspannen	1	2	3	4
16. Ik voel me tevreden	1	2	3	4
17. Ik maak me zorgen	1	2	3	4
18. Ik voel me gejaagd	1	2	3	4
19. Ik voel me evenwichtig	1	2	3	4
20. Ik voel me prettig	1	2	3	4

Einde vragenlijst.



Appendix B

The narrative used during the induction of anticipatory state social anxiety, by means of the speech task. The subject was told the following story:

“Imagine the following situation clearly. You and three fellow students collaborate on an academic report. It goes well and you receive high course credit for the end result. However, your peers aren’t satisfied with your effort. They accuse you of misusing their effort and state that you haven’t contributed anything to the end result. They don’t want you to receive the same credit for this report, because you aren’t entitled to it. They have already contacted the supervisor of this project. The supervisor wants to meet with the four of you to talk about this situation. During this conversation you will have the opportunity to defend yourself against this accusation. Now, you have to come up with credible arguments to convince your supervisor that you actually did put effort in the end result and that your fellow students are wrong.”

After this narrative, the subject was told that she had five minutes to prepare herself for a plea. After these five minutes she had to give her plea in front of a video camera. The subject was told that the tape would be judged by a panel of experts on the degree of credibility and self-assurance shown by the subject. In reality, the plea never occurred. It was part of the induction of a state of anticipatory social anxiety.