



Centre for Systems Neuroscience
Hannover, Germany

PROCESSING OF EMOTIONAL INFORMATION IN PATIENTS WITH PRIMARY CERVICAL DYSTONIA

A Dissertation submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy (PhD) at the Center for Systems Neuroscience, awarded by the University of Veterinary Medicine Hannover, Hannover, Germany

BY

Zornitza T. Nikolova, MD
Born in Sofia, Bulgaria

Hannover, 2009

Thesis Supervisor:

Prof. Dr. med. Reinhard Dengler

Referees:

1. Prof. Dr. med. Reinhard Dengler
2. Prof. Dr. med. Eckart Altenmüller
3. Prof. Dr. Elke Zimmermann

External referee:

PD Dr Sonja A. Kotz

Max Planck Institute for Human Cognitive and Brain Sciences

Stephanstraße 1A,

04103 Leipzig,

Germany

Date of final exam: October 24th 2009

This work was supported by Marie Curie Early Stage Training Fellowship (EST) of the European Community's Sixth Framework Programme under contract number MEST-CT-2005-021014.

DEDICATION

*To my parents Rada and Tashko for
their support and encouragements
and unconditional love.*

Thank you.

Statement of research

Herewith I declare that I autonomously carried out the PhD thesis entitled “Processing of emotional information in patients with primary cervical dystonia”. No third party assistance has been used.

I did not receive any assistance in return for payment by consulting agencies or any other persons. No one received any kind of payment for direct or indirect assistance in regard to the content of the submitted thesis.

I conducted the project at the Department of Neurology with Clinical neurophysiology, in Hannover Medical School, Hannover, Germany.

The thesis has not been submitted elsewhere for an exam, as thesis or for evaluation in a similar context. Hereby I affirm the above statements to be complete and true to the best of my knowledge.

Hannover

Zornitza Nikolova

July 2009

Summary

Primary dystonia is the third most common movement disorder in humans. It is being described as a syndrome of sustained muscle contractions, frequently causing twisting and repetitive movements or abnormal postures (Fahn, 1988). Dystonia is considered to manifest primarily with pure motor deficit, however, recent studies have shown that the motor disturbances might be accompanied by cognitive impairments and psychiatric comorbidity. Despite the growing interest in the non-motor manifestations, emotional information processing in dystonia is yet insufficiently investigated. Previous research has demonstrated a deficient recognition of emotional faces in patients with primary focal dystonia but it remains unclear if affective speech recognition in these patients is also affected. Although not fully understood, the pathophysiology of dystonia is ascribed mainly to basal ganglia dysfunction. Besides the motor control, striatopallidal structures are known to implement also non-motor functions including processing of emotional information and in particular the recognition of emotional prosody and facial expressions of affect. Emotional prosody, a suprasegmental feature of language, enables the listener to infer the internal affective state of a speaker regardless of the semantic content of speech. Therefore, emotional prosody recognition is very important for everyday social interaction. The concept that the basal ganglia are involved into circuits subserving the processing of emotional prosodic information is being supported by numerous studies with Parkinson's (PD) and Huntington's (HD) disease patients, who have consistently shown impairment in emotional speech comprehension.

By employing event related brain potentials (ERPs) technique and behavioral studies, we investigated emotional prosody recognition in patients with primary cervical dystonia (CD, n=30) and compared the results with a healthy control group (HC, n=30). The participants were instructed to judge the emotional tone of auditory presented words according to their valence (negative-positive) or arousal (calm-excited) in two experimental conditions by pressing one of three keyboard buttons. The results revealed a significantly poorer performance of CD patients in classifying the emotional prosody. The analysis of hit rates and reaction times disclosed a significantly less accurate performance of CD patients in judging especially angrily intonated words. Moreover, the elicited ERPs showed smaller P3b amplitudes in CD across all investigated emotions (angry, happy, relaxed, and sad). Importantly, the deficient recognition of emotional intonation was observed only when the CD patients had to classify the stimuli according to their valence while in the arousal task no group differences were found.

Another aspect of the present research was to consider the psychological status and personality profile of CD patients and determine possible correlations with the performance of emotional prosody recognition. Interestingly, our results did not demonstrate a significant correlation between the performance in the emotional prosody recognition task and neither the psychological status (BDI, SCL-90-R general distress index, depression and anxiety scores) nor the severity, duration and age of onset of CD, indicating that the emotional processing deficit is rather primary in nature and not a consequence of the chronic disease. Moreover, our findings designated some specific personality features that seem to be predominating in CD patients. Evaluation of the personality profile disclosed prominent psychosomatic complaints, accentuated strain and emotionality traits in the patient group as well as less

pronounced extroversion characteristics. This profile appears to be characteristic for the patients suffering from cervical dystonia but did not show any correlation with the emotional processing deficit.

Taken together the findings of the present study disclose a deficit in emotional prosody comprehension in patients with primary cervical dystonia. Given that the prosodic deficit involved all investigated emotions it appears that the disturbed processing of emotional prosodic information in CD is rather general in nature than restricted to certain emotional categories. Most importantly, the recognition of valence dimension appears to be explicitly impaired. Assuming that the processing of emotional valence is subserved by the mesolimbic dopaminergic system, as proposed by [Posner et al., \(2005\)](#), it seems plausible that the recognition of the valence dimension is preferentially affected in CD. In addition, dystonia patients displayed more often anxiety, depression and specific personality traits showing however no correlation with the performance in emotional prosody recognition. Hence, our findings provide further evidence for the essential role that the basal ganglia implement in emotional prosody processing and also emphasize the importance to recognize the non-motor symptoms in patients with primary focal dystonia as complementary to the motor deficit.

Zusammenfassung

Die primären Dystonien gehören zu den drei häufigsten Bewegungsstörungen. Unter einer Dystonie werden prolongierte Muskelkontraktionen verstanden, die zu repetitiven Bewegungen oder abnormen Haltungen führen (Fahn, 1988). Wenngleich die genannten Auswirkungen auf die Motorik im Vordergrund der Erkrankung stehen, konnten jüngere Studien belegen, dass zusätzlich kognitive Einschränkungen sowie affektive Störungen begleitend auftreten können. Auch wenn diese nicht-motorischen Symptome zunehmendes Interesse erhalten, wurde insbesondere der Bereich der Emotionsverarbeitung bislang wenig untersucht. Es gibt Arbeiten, die auf eine eingeschränkte Verarbeitung emotionaler Gesichtsausdrücke bei Patienten mit primärer fokaler Dystonie hinweisen, ob dies auch auf die Verarbeitung emotionaler Sprache zutrifft ist bislang ungeklärt. Als pathophysiologische Ursache der primären Dystonien wird eine Fehlfunktion der Basalganglien angenommen. Neben ihrer Bedeutung für das motorische System übernehmen die Basalganglien und ihre Verbindungen wichtige nicht-motorische Aufgaben zu denen auch die Emotionsverarbeitung zählt. Die Annahme, dass die Basalganglienschleifen an der Verarbeitung emotionaler Prosodie beteiligt sind, wird gestützt durch Studien mit Patienten die an den Bewegungsstörungen Morbus Parkinson und Morbus Huntington erkrankt sind. Indem über die Bewertung der emotionalen Prosodie oder Sprachmelodie unabhängig von dem Sprachinhalt (Semantik), auf das emotionale Befinden des Sprechers geschlossen werden kann, erfüllt diese einen wichtigen Aspekt der zwischenmenschlichen Kommunikation.

Mittels Ableitung der Hirnstromkurve und Berechnung sogenannter ereigniskorrelierter Potentiale (EKP) untersuchten wir die Verarbeitung emotionaler Prosodie bei Patienten mit primärer cervikaler Dystonie (CD, n=30) im Vergleich zu einer Gruppe gesunder Kontrollprobanden (CD, n=30). Die Teilnehmer wurden instruiert die auditorisch präsentierten Worte nach ihrer emotionalen Prosodie zu beurteilen. In der sogenannten Valenzaufgabe sollte das gesprochene Wort als negativ oder positiv und in der Arousalauftgabe als erregt oder ruhig klingend beurteilt werden. Zur Beantwortung wurde einer von drei Antwortknöpfen gedrückt. Die Ergebnisse zeigen, dass die Dystoniekpatienten bei der Aufgabe die Valenz eines gesprochenen Wortes zu beurteilen, schlechter abschneiden. Hierbei zeigt die Analyse der korrekten Antworten als auch der Reaktionszeiten, dass Patienten insbesondere bei der Einschätzung der Valenz ärgerlich gesprochener Worte Schwierigkeiten aufweisen. Darüber hinaus zeigt sich bei den EKP eine verminderte Amplitude der P3b Komponente in der Patientengruppe für alle untersuchten Emotionen (ärgerlich, fröhlich, traurig, entspannt) – ebenfalls nur in der Valenzaufgabe.

Ein weiterer Aspekt der vorliegenden Arbeit war, das Persönlichkeitsprofil sowie den psychologischen Status der Patienten mit cervikaler Dystonie zu erfassen (BDI, SCL-90-R, Depressions- and Ängstlichkeitswerte) und mit dem Abschneiden bei der Verarbeitung emotionaler Prosodie zu korrelieren. Die Ergebnisse weisen jedoch nicht auf eine solche Korrelation hin. Auch die Schwere und Dauer der Erkrankung sowie das Alter bei Beginn der Erkrankung zeigten keine solche Korrelation. Insgesamt spricht dies dafür, dass das gefundene Defizit der Verarbeitung emotionaler Prosodie nicht als Konsequenz der chronischen, den Alltag einschränkenden

Bewegungsstörung gesehen werden kann. Auch die Persönlichkeitsmerkmale - wie psychosomatische Beschwerden, Zeichen einer erhöhten Belastung, verminderte Extroversion - die wir gehäuft bei Patienten mit cervikaler Dystonie fanden korrelierte nicht mit der Leistung in der emotionalen Prosodieverarbeitung.

Zusammenfassend lässt sich sagen, dass die Ergebnisse der vorliegenden Arbeit ein Defizit der Verarbeitung emotionaler Prosodie bei Patienten mit cervikaler Dystonie belegen. Insbesondere die Verminderung der Amplitude der P3b Komponente, die sich bei allen untersuchten emotionalen Färbungen (ärgerlich, fröhlich, traurig, entspannt) fand, spricht gegen die Hypothese das nur die Verarbeitung spezifischer Emotionen betroffen ist. Interessanterweise zeigten sich diese Veränderungen aber nur bei der Aufgabe, die Valenz der angebotenen Worte zu beurteilen. Geht man davon aus, dass bei der Valenzbeurteilung dem mesolimbischen dopaminergen System eine wichtige Bedeutung zu kommt, wie es von [Posner und Kollegen \(2005\)](#) postuliert wurde, lässt sich erklären warum Dystonieklienten insbesondere bei der Beurteilung der Valenz Schwierigkeiten aufweisen. Insgesamt belegen die Ergebnisse erneut die wichtige Rolle der Basalganglien und ihrer Verbindungen bei der Verarbeitung emotionaler Prosodie und verdeutlichen, wie wichtig es ist bei Patienten mit primär fokaler Dystonie auch nicht motorische Symptome zu beachten, die letztlich zu einer weiteren Einschränkung der Lebensqualität der Patienten führen können.

Contents

CHAPTER 1

GENERAL INTRODUCTION

1. DYSTONIA.....1

 1.1 HISTORICAL OVERVIEW DYSTONIA1

 1.2 CLINICAL FEATURES2

 1.3 CLASSIFICATION2

 1.4 EPIDEMIOLOGY AND AETIOLOGY3

 1.5 PATHOPHYSIOLOGY HISTORICAL OVERVIEW DYSTONIA.....3

 1.6 IS DYSTONIA A PURE MOTOR DISORDER?5

2. EMOTIONS7

 1.1 WHAT IS EMOTION.....7

 1.2 MODELS OF EMOTION.....9

 1.3 COMMUNICATING EMOTIONS10

 1.4 PROCESSING OF EMOTIONAL PROSODY.....11

1.5 NEURAL CORRELATES OF EMOTIONAL PROCESS	13
3. OBJECTIVE	16
REFERENCES	19

CHAPTER 2

DEFICIENT RECOGNITION OF EMOTIONAL PROSODY IN PRIMARY FOCAL DYSTONIA

1.1 ABSTRACT	27
1.2 INTRODUCTION.....	28
1.3 SUBJECTS AND METHODS.....	30
1.4 STIMULI AND EXPERIMENTAL DESIGN	31
1.5 PSYCHOLOGICAL STATUS AND PERSONALITY PROFILE.....	32
1.6 STATISTICAL EVALUATION.....	33
1.7 RESULTS	33
1.8 DISCUSSION.....	37
REFERENCES.....	42

CHAPTER 3

DEFICIENT PROCESSING OF EMOTIONAL VALENCE IN PRIMARY CERVICAL DYSTONIA: ERP STUDY

1.1 ABSTRACT	45
1.2 INTRODUCTION.....	46
1.3 METHODS	49
1.3.1 SUBJECTS.....	49
1.3.2 STIMULI AND EXPERIMENTAL DESIGN.....	50
1.3.3 ERP ACQUISITION AND ANALYSIS.....	53
1.4 RESULTS.....	54
1.4.1 VALENCE CONDITION - P3B COMPONENT.....	54
1.4.2 AROUSAL CONDITION - P3B COMPONENT.....	55
1.4.3 BEHAVIORAL DATA.....	56
1.5 DISCUSSION.....	58
REFERENCES.....	64

CHAPTER 4

GENERAL DISCUSSION.....	67
REFERENCES.....	75
ACKNOWLEDGEMENTS	82

Introduction

1. Dystonia

1.1 Historical overview

Dystonia was first described in 1911 by the German neurologist Hermann Oppenheim who had observed a disorder presented with uncontrollable and bizarre twisting movements eventually progressing in fixed abnormal postures. The illness was initially called dystonia musculorum deformans and was later referred to as *primary torsion dystonia* (Grundmann, 2005). Dystonia has been originally considered a manifestation of a psychiatric disorder and the question of its functional or organic origin has been largely discussed among the neuropsychiatric community. Actually, more than half a century passed before the primary torsion dystonia was recognized as a distinct entity and very recently physicians have accepted that this seemingly bizarre condition was due to an organic brain disease (Marsden et al. , 1976). Although long suspected, the hereditary basis of dystonia was finally acknowledged in the late 1960s when Zeman and Dyken (1967) have documented the existence of an autosomal dominant (AD) form of the disease. As a result, after all these years, a committee consisting of members of the scientific advisory board of the Dystonia Medical Research Foundation developed the following definition that is still in use: “Dystonia is a syndrome of sustained muscle contractions, frequently causing twisting and repetitive movements, or abnormal postures” (Fahn, 1988).

1.2 Clinical features

Dystonia is currently thought to represent a heterogeneous syndrome resulting from involuntary concomitant contraction of agonist and antagonist muscles, with overflow of unwanted muscle contractions into adjacent muscles (Tarsy and Simon, 2006). The prolonged muscle contractions cause sustained, repetitive twisting movements and abnormal postures of the affected body part/s that may become fixed in the advanced cases. Tremor and pain may be present. The abnormal movements can occur during voluntary activity (action dystonia) and are sometimes task-specific. Some localized dystonias respond to simple sensory tricks such as slightly touching the affected body part (geste antagoniste).

1.3 Classification

Dystonia has different classifications according to the age of onset, body distribution, and aetiology (Fahn et al. , 1998). *Early-onset* dystonia usually develops in childhood and has a progressive course with tendency to generalise, while *adult-onset* forms normally start after age of 25 years and have a limited tendency to spread to neighbouring body regions (Fahn et al., 1998). The aetiological classification includes two major categories according to the underlying cause: *primary* (idiopathic) and *secondary* (symptomatic) dystonia. *Primary dystonia* is of unknown cause, except for some cases with identified genetic mutations (Bressman, 2004), and does not display any structural abnormalities of the CNS. *Secondary dystonia* has a certain exogenous, structural or metabolic cause with lesions involving most often the basal ganglia or thalamus (Marsden et al. , 1985; Pettigrew and Jankovic, 1985). Alternatively, dystonia is classified according to its body distribution as *focal*, *segmental*, *hemidystonia*, and *generalized* dystonia (idiopathic torsion dystonia).

Focal dystonias may affect each body part but the most common forms include focal hand dystonia (FHD), blepharospasm (BSP) involving the external eye muscles and cervical dystonia (CD) affecting the neck region.

1.4 Epidemiology and aetiology

Dystonia currently represents the third most common movement disorder in humans with highest prevalence of primary dystonias (Defazio et al. , 2007, 2004). The focal adult-onset forms occur ten times more often than the generalized early-onset forms (Greene et al. , 1995) and the cervical dystonia (CD), being the main focus of the present study, represents the most common form of the adult-onset focal dystonias (Defazio et al. , 2004). *Primary generalized torsion dystonia* is known to have a genetic cause and is inherited exclusively in an autosomal dominant manner with reduced (30%) penetrance (Burke et al. , 1986; Pauls and Korczyn, 1990). It arises from GAG deletion in DYT1 gen (Ozelius et al. , 1997) that is responsible for coding the Torsin A protein, a brain protein of unknown function with highest concentrations in the substantia nigra (De Carvalho Aguiar and Ozelius, 2002). *Primary focal dystonia* is thought to be partly genetic due to its aggregation within certain families (Brancati et al. , 2002; Defazio et al. , 2003) but most cases appear to be sporadic and the aetiology appear to combine genetic and environmental factors (Defazio et al., 2007).

1.5 Pathophysiology

The pathophysiology of primary dystonia is rather complex but the main pathogenic mechanism is thought to arise from basal ganglia dysfunction. More specifically, an overactivity of the direct striatopallidal pathway resulting in reduced output of the

internal globus pallidus and increased excitatory thalamic input to the cortex (Berardelli et al. , 1998, Defazio et al., 2007), accounts for the altered inhibitory control at different levels of the motor system causing decreased intracortical inhibition and abnormal regulation of brainstem and spinal cord inhibitory interneuronal mechanisms. Additionally, the role of an altered sensory feedback in the generation of dystonic



Fig.1 Pathophysiology of dystonia: reduced inhibitory GPi output and increased excitatory thalamic input to the cortex; GPe, external pallidum; GPi, internal pallidum; STN, subthalamic ucleus; SNc, substantia nigra compacta; SNr, substantia nigra reticulate; DA, dopamine; GABA, fgamabutiric acid, Glu - glutamate.

movements has been emphasized by a number of studies, suggesting a defective sensorimotor integration and maladaptive plasticity as possible pathophysiological mechanisms contributing to the development of dystonia (Defazio et al., 2007). Using a variety of neuroimaging techniques like volumetric imaging, voxel-based morphometry functional MRI and PET numerous studies have recently reported structural abnormalities of the basal ganglia (Defazio et al., 2007) that are similar in several forms of adult - onset focal dystonias, namely putaminal enlargement (Black et al. , 1998), increased striatopallidal grey matter density (Etgen et al. , 2006; Garraux et al. , 2004; Draganski et al. , 2003), enhanced bilateral BOLD signal of putamen, caudate nucleus, internal globus pallidus and lateral thalamus (Peller et al. , 2006) and increased metabolism in lentiform nucleus (Magyar-Lehmann et al. , 1997; Galardi et al. , 1996). This body of evidence not only brings insight to basal ganglia involvement in the pathophysiology of primary focal dystonias but also suggests that besides the functional

abnormalities subtle structural changes of the striatopallidal structures might additionally contribute to the pathogenesis of dystonia. The role of dopamine in dystonia is yet poorly understood (Berardelli et al., 1998). However one of the most important breakthroughs is the discovery that dopa-responsive dystonia arises from mutations in a gene coding for an enzyme involved in L-dopa synthesis causing a subsequent failure of dopamine formation (Furukawa et al. , 1998). Levodopa replacement therapy in patients with dopa-responsive dystonia leads to a remarkable relief of the symptoms. Moreover, recent functional imaging studies (SPECT/PET) have documented bilateral reduction of postsynaptic dopamine D2 receptor binding in the striatum of patients with the main forms of late-onset dystonia (Naumann et al. , 1998; Horstink et al. , 1997; Perlmutter et al. , 1997; Hierholzer et al. , 1994) suggesting that a dopamine depletion might be involved in the pathophysiology of the disease. However, other studies of striatal dopa uptake have revealed various dopamine levels in primary dystonia (Playford et al. , 1993; Otsuka et al. , 1992; Eidelberg et al. , 1995) indicating that the disorder may occur with different brain levels of dopamine (low, high or intermediate). Therefore, the exact role of dopamine in the pathogenesis of dystonia remains unexplained (Berardelli et al., 1998).

1.6 Is dystonia a pure motor disorder ?

In the recent years the common belief that primary dystonia is a pure motor disorder has been challenged and the interest in none motor manifestations of the disorder is continuously growing. Evidence indicates that the motor deficit in primary dystonia is accompanied by cognitive disturbances and psychiatric comorbidity. Scott et al. (2003) have demonstrated the presence of a selective attentional – executive

cognitive deficit in patients with primary dystonia. Similar cognitive abnormalities in dystonia have been corroborated by other researchers (Duane and Vermilion, 2004; Duane, 2004; Duane and Vermilion, 2002), although few studies could not bring such evidence (Jahanshahi et al. , 2003; Balas et al. , 2006). The cognitive deficit in dystonia patients appears to be subtle and perhaps not significantly disabling in everyday life (Scott et al. , 2003). However, psychiatric comorbidity has been shown to have a significant impact on quality of life, and treating only the motor symptoms of dystonia does not improve this fact (Muller et al. , 2002). Converging evidence points to a higher prevalence of psychiatric disturbances in dystonia population. The concomitant psychiatric conditions that are commonly reported in dystonia include depression (Miller et al. , 2007; Heiman et al. , 2007; Lauterbach et al. , 2004; Moraru et al. , 2002; Wenzel et al. , 1998; Gundel et al. , 2003; Lewis et al. , 2008), anxiety (Lauterbach et al., 2004; Jabusch et al. , 2004; Gundel et al., 2003; Moraru et al., 2002; Wenzel et al., 1998), obsessive - compulsive disorders (Cavallaro et al. , 2002; Wenzel et al., 1998; Broocks et al. , 1998; Bugalho et al. , 2006) and social phobia (Ozel-Kizil et al. , 2008; Gundel et al. , 2001; Gundel et al., 2003; Lauterbach et al., 2004). There is no clear consensus about the cause of this increased prevalence but there might be a common pathological background linking psychiatric illness and dystonia (Heiman et al. , 2004; Gundel et al., 2003; Cavallaro et al., 2002; Saunders-Pullman et al. , 2002).

2. Emotions

2.1 What is emotion?

Nature has developed emotions over thousands of years of evolution. As a result, they have evolved as adaptive survival mechanism having the potential to serve as a delicate and sophisticated internal guidance system that alerts us when our natural human need is not being met. There is still no unified definition of emotions but it is well accepted that they comprise several components. According to [Plutchik \(1984\)](#) by *emotion* we refer to reactions to an appropriately evocative stimulus involving cognitive appraisal (or perception), expressive motor behaviour, subjective experience (or feelings), physiological arousal, and goal directed behaviour.

Charles Darwin, a pioneer in emotional research, was the first who described the relation between emotional expression and the internal state of its sender ([Darwin, 1965](#)) suggesting that human emotions implement adaptive functions and adjust bodily responses to various challenges in the surrounding environment. The first popular theory of emotions, known as James-Lange theory is named after the two scientists that independently contributed to its development, William James ([James, 1884](#)) and Carl Lange ([Lange, 1885](#)). The authors argued that stimuli eliciting emotions first induce changes in the viscera and the autonomic nervous system and subsequently the perception of these signals produces emotional experience. Later on, Walter Cannon ([Cannon, 1927](#)) together with Philip Bard ([Bard, 1928](#)) challenged the James-Lange theory and concluded that the visceral output to the brain is too weak and insufficient to evoke emotional experience. Cannon noted that emotions da

implicate primarily adaptive functions that had evolved to ensure survival of the organism and represent one of the strongest motivational forces of human behavior. Whereas James argued that emotional behaviour often precedes or defines the emotion, Cannon and Bard claimed that the emotion arises first and then stimulates typical behaviour. In the early 1960s, following the “cognitive revolution” in the field of psychology, Stanley Schachter and Jerome Singer devised a new theory of emotion that took into account the influence of cognitive factors. With regard to the previous theories, the scientists claimed that the variety of emotions is not matched by an equal variety of visceral patterns and concluded that cognitive factors may be major determinants of emotional states. Moreover, it was proposed that experiencing an emotion would require both emotional arousal and cognitive activity (Schachter and Singer, 1962). In parallel, Magda Arnold developed her “cognitive theory”, which specified that the first step in emotion is an appraisal of the situation. According to Arnold, the initial appraisal starts the emotional sequence and leads to both the appropriate actions and the emotional experience itself. Therefore the physiological changes, recognized as important, accompany but do not initiate the actions and experiences. Further on, David Lazarus attempted to explain the human behavior by looking at the structure of the brain and suggested that cognitive appraisal of the situation in the form of judgments, evaluations or thoughts, is essential for an emotion to occur (Lazarus, 1991). He argues that an emotion-evoking stimulus first triggers a cognitive appraisal (conscious or unconscious assessment of the situation) which is thereafter followed by the emotion and physiological arousal. Lazarus’s theory emphasizes the importance of cognition for emotional experience, which is dependent on how the individual evaluates the impact of an event on his/her self well-being.

2.2 Models of emotion

Research on basic emotions began in the early 1860s with Darwin's efforts to reveal how specific mental states seek expression and therefore cause specific sets of human emotional behavior. He has applied an innovative approach by using photographs from real life or posed by professional actors to establish which facial expressions were reliably

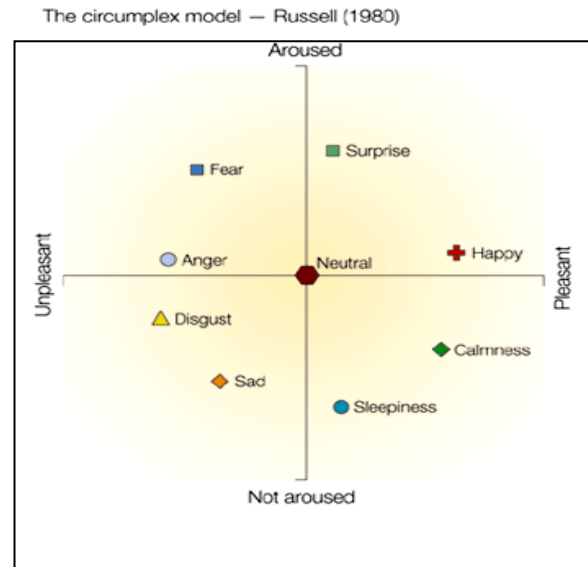


Fig.2 Circumplex model of affect: the horizontal axis represents the valence dimension and the vertical axis, the arousal/activation dimension. Figure adopted

recognized as indicating certain emotions. Darwin proposed the view that all emotions are innate, and there are not or only small, differences in emotional expression between different cultures (Darwin, 1872). His ideas were later on developed by numerous basic emotion theorist (Tomkins, 1962, 1963, 1984; Eckman et al. , 1972, 1973, 1999; Izard, 1977, 1993; Panksepp, 1998 Plutchik, 1980). Paul Ekman, a pioneer in the study of emotions, together with Friesen and Ellsworth (Eckman et al. 1972) defined six basic emotions *anger, disgust, fear, joy, sadness, and surprise* that can be reliably recognized from facial expressions. According to the model of basic emotions humans are evolutionarily endowed with a discrete and limited set of fundamental emotions, each causing a distinct pattern of physiological, psychological and behavioral responses and each arising from activation within unique neural pathways of the central nervous system (Ekman, 1992; Panksepp, 1998; Tomkins, 1962, 1963). However, studying the subjective experience of emotion, researchers have noted that individuals rarely describe feeling a specific positive emotion without also claiming to feel other positive emotions positive emotion (Watson and Clark, 1992)

Difficulty in describing one's own emotions suggests that individuals do not experience emotions as isolated discrete entities but rather recognize them as ambiguous and overlapping experiences. Indeed emotions seem to lack the discrete borders that would clearly differentiate one emotion from another (Russell and Fehr, 1994). Thus, the extensive research on emotions yielded the development of dimensional models of emotion regarding affective experiences as a continuum of highly interrelated and often ambiguous states. In the two-dimensional (2-D) models (Larsen and Diener, 1992) of affective experience dimensions have been conceptualized in different ways: as dimensions of positive and negative affect (Watson and Clark, 1992), tension and energy (Thayer, 1989), approach and withdrawal (Lang et al. , 1998) or valence and arousal (Russell, 1980). Despite the differing descriptive labels applied to these dimensions, the 2-D structure is found consistently across a large number of studies (Posner et al. , 2005b). Currently well recognized is Russell's circumplex model of affect (Russell, 1980) (Fig 2) according to which each emotion can be interpreted as a linear combination of different degree of two primary dimensions, *valence* (positive to negative continuum) and *arousal* (calmness to excitement continuum). Interpreting Russell's model of affect, Posner et al. (2005) suggest that all affective states arise from two independent neurophysiological systems, the mesolimbic dopaminergic system underlying the valence and the reticular formation responsible for the arousal processing.

2. 3 Communicating emotions

Emotions are communicated between humans in various ways through visual and auditory communication channels. Thus affect may be expressed and perceived by facial emotional expressions, gestures, postures, vocal exclamations or verbal

utterances. A large body of research based on the theory of discrete emotions has been performed mainly with emotional faces indicating that facial expressions are associated with universal affective states recognizable across cultures. (Tomkins 1962, 19963; Ekman et al. , 1969, 1972,1973,1987; Izard, 1994 , 1998; Panksepp, 1998). Likewise, the vocal communication channel also provides useful and reliable information for decoding the affective state of the sender. One important aspect of vocal communication is the prosodic contour of a vocal emotional message, also referred to as emotional prosody. The emotional prosody or melody of speech is a suprasegmental feature of the language inferring the internal state of the speaker regardless of the semantic meaning. The expression of emotional prosody is a spontaneous involuntary phenomenon conveying the inner affective state of the speaker (Wambacq and Jerger, 2004) and its recognition is a very important aspect of human social interaction. Affective prosody recognition depends on the analysis of different acoustic cues conveying the emotional prosody, among which the most important appear to be intensity, timing and fundamental frequency (Banse and Scherer, 1996).

2.4 Processing of emotional prosody

One of the most debated questions in the field of emotional prosody research involves the underlying neural correlates of the affective prosody processing. Recent studies using intracranial recordings (Liegeois-Chauvel et al. , 2004) and functional imaging (Zatorre and Belin, 2001) have provided compelling evidence for a hemispheric specialization in the auditory processing. It has been suggested that the left and right hemisphere differ in processing of temporal and spectral auditory information with the right hemisphere specialized in pitch processing and the left

hemisphere responsible for temporal information processing. Another concept of hemispheric specialization (Peretz et al. , 1994) suggests that the processes associated with identification of linguistic auditory objects are lateralized to the left hemisphere (Parker et al. , 2005) while the paralinguistic aspects of vocal processing are lateralized to the right hemisphere (Belin et al. , 2004). Besides interhemispheric differences, a differential involvement of intrahemispheric brain areas in the processing of emotional information is also disputed. Based on various research findings it has been postulated that an emotional processor in the right hemisphere functions as an analog to the speech processor in the left hemisphere (Ross and Monnot, 2008; Goodglass and Kaplan, 1983; Ross, 1981). According to this theory, anterior brain structures are involved in expressive tasks, whereas posterior areas contribute to stimulus perception (Ross, 1981,1997; Cancelliere and Kertesz, 1990; Starkstein et al. , 1994). A very comprehensive model of emotional-prosodic processing has been proposed by Schirmer and Kotz (2006) suggesting that vocal emotional comprehension consists of hierarchically organized sub-processes that are differentially represented in the brain. According to this model, auditory cortex mediates the analysis of acoustic information (Fig. 3a, stage 1) and codes frequency and amplitude information, as well as their temporal envelope within the first 100 ms following stimulus onset. Hemispheric differences in temporal resolution mediate a right hemisphere lateralization for spectral processing and a left hemisphere lateralization for temporal processing. Following basic acoustic processing, vocal emotional expressions recruit areas along the auditory processing stream that encode the emotional significance of vocalizations (Fig. 3a stage 2). During this processing stage, different acoustic cues that convey emotional information are integrated as processing progresses towards the anterior superior temporal sulcus (STS). Activity at

the level of the STS seems lateralized to the right hemisphere and occurs with a latency of approximately 200 ms. Emotional significance derived at the level of the anterior STS is then available for higher order cognitive processes, such as evaluative judgments mediated by the right inferior and orbitofrontal cortex or effortful semantic processing associated with banter and sarcasm mediated by left inferior frontal cortex (Fig. 3a, stage 3).

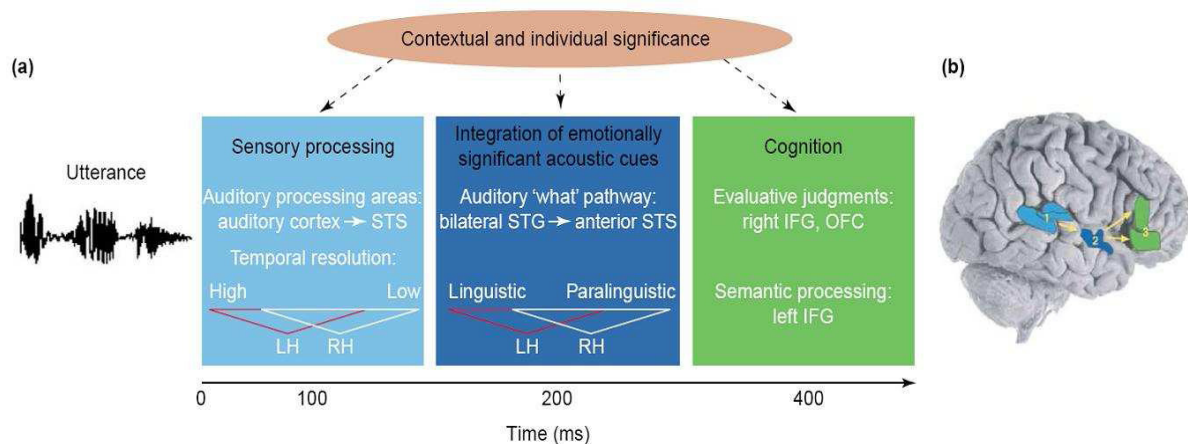


Figure 2: (a) Three-stage working model for the processing of emotional prosody. Sensory processing (Stage 1): Acoustic analysis is mediated by bilateral auditory processing areas. Integration (Stage 2): Processing along the auditory “what” pathway integrates emotionally significant acoustic information to derive an emotional “gestalt.” This pathway projects from the superior temporal gyrus (STG) to the anterior superior temporal sulcus (STS) and might be lateralized to the right hemisphere (RH). Cognition (Stage 3): Emotional information derived at the level of the STS is made available for higher-order cognitive processes. For example, explicit evaluative judgments of emotional prosody are mediated by the right inferior gyrus (IFG) and orbitofrontal cortex (OFC), whereas the integration of emotional prosody into language processing recruits inferior frontal gyrus in the left hemisphere (LH). Contextual or individual significance might facilitate or enhance processing at any of the three stages. (b) Schematic presentation of brain areas implicated in vocal emotional processing in a right sagittal view: primary, secondary, and tertiary auditory cortex (light blue) extending to the anterior portion of the superior temporal sulcus (dark blue), from where projections reach inferior frontal gyrus and orbitofrontal gyrus (green). Arrows (yellow) indicate presumed processing directions (colors/numbers correspond to the processing stages outlined in (a)). Figure adopted from Schirmer and Kotz, 2006 (Copyright: Elsevier 2009).

2.5 Neural correlates of emotional processing

Considerable research has been dedicated to the concept of right hemisphere specialization in processing of emotional information and especially affective prosody (Blonder et al. , 1991; Borod et al. , 1998, 2002, 1985; George et al. , 1996; Pihan et al. , 1997; 2000; Buchanan et al. , 2000; Mitchell et al. , 2003; Mitchell, 2006; Esslen et al. , 2004; Breitenstein et al. , 1998; Bowers et al. , 1987; Darby, 1993; Starkstein et al., 1994; Ross et al. , 1997). However, the widely accepted notion of right hemisphere dominance in the identification of facial and vocal emotions has been recently challenged. Several investigations during the last decade could not support a right hemisphere superiority for facial expressions (Cancelliere and Kertesz, 1990; Gainotti, 1989; Stone et al. , 1996; Weddell, 1989) as well as affective prosody (Cancelliere and Kertesz, 1990; Van Lancker and Sidtis, 1992; Pell, 1998, 2006). In addition to right cortical areas, it appears that left cortical regions are also recruited in processing of emotional prosodic information (Adolphs, 2002; Breitenstein et al., 1998; Kotz et al. , 2003; Mitchell et al., 2003; Grandjean et al. , 2005; Wildgruber et al. , 2005, 2004, 2002; Cancelliere and Kertesz, 1990) suggesting that the right hemisphere's participation in emotional prosody constitutes a *relative* rather than an *absolute* dominance in this processing domain. One further theory of emotional processing, the valence hypothesis, postulates a dominance of the right hemisphere in the processing of negative emotions, whereas the left hemisphere is more involved in the comprehension of positive emotions (Silberman and Weingartner, 1986; Davidson, 1995; Davidson and Tomarken, 1989; Canli et al. , 1998; Gagnon and Peretz, 2000). The majority of studies with neurological patients, however, have not provided support for this differentiation (Borod, 1992). Recently, attention has been brought to the important role of the basal ganglia in emotion processing. Cancelliere and Kertesz, 1990 have reported that patients with cortical lesions and additional damage to the

basal ganglia and/or the anterior temporal lobes show the most pronounced deficits in emotional judgements, independent of the lesion side. Further evidence for the role of basal ganglia in processing of emotions is provided by studies describing prosodic and facial comprehension disturbances in patients with Parkinson's disease, (Ariatti et al. , 2008; Dara et al. , 2008; Schroder et al. , 2006; Yip et al. , 2003; Breitenstein et al. , 2001, 1998; Pell and Leonard, 2003; Pell, 1996; Suzuki et al. , 2006; Lloyd, 1999; Benke et al. , 1998), Huntington's diseases (Speedie et al. , 1990; Sprengelmeyer et al. , 1996), patients with subcortical brain lesions (Paulmann et al. , 2008; Yip et al. , 2004; Calder et al. , 2004) and healthy control subjects (Kotz et al., 2003; Wildgruber et al. , 2002; Bach et al. , 2008). Emotions are thought to differ in distinct patterns of changes in motor expressions, physiology and subjective feelings (Scherer, 2000). However the question whether the recognition of distinct basic emotions is associated with dissociable neuronal systems (Sprengelmeyer et al. , 1998) remains elusive. The concept of separable emotion specific neuronal networks has gained support from numerous studies on processing of emotional facial expressions. Converging evidence point to specific anatomical structures involved in processing of fear and disgust. The amygdala is believed to be implicated in processing of fearful facial expressions (Adolphs et al. , 1994, 1995, 2005; Calder et al. , 1996; Broks et al. , 1998; Breiter et al. , 1996; Morris et al. , 1996a; Whalen et al. , 1998; Phillips et al. , 1998) and basal ganglia and insula in processing expressions of disgust (Sprengelmeyer et al., 1996; Gray et al. , 1997; Phillips et al. , 1997, 1998; Rinnerthaler et al. , 2006). Based on meta-analysis across various imaging studies Phan et al. , 2002(2002) have proved evidence that separate brain regions are involved in different aspects of emotions. The authors suggest that fear processing is

specifically associated with the amygdala, disgust with the basal ganglia and insular cortex, sadness with the the subcallosal anterior cingulate cortex and happiness induction again with the basal ganglia.

Findings of specific brain regions implementing specialized functions in recognition of vocal expressions seem to be less convergent. Nevertheless bilateral amygdala damage has been associated with selectively impaired recognition of fearful (Phillips et al., 1998; Scott et al. , 1997; Morris et al. , 1999; Isenberg et al. , 1999) and angry vocalizations (Scott et al., 1997), providing evidence for functional specialization within neural systems processing vocal emotion, though not confirmed by other studies (Adolphs and Tranel, 1999; Anderson and Phelps, 1998). Furthermore, ratings of vocal expressions of anger have been shown to be deficient in patients with ventral striatum lesions (Calder et al., 2004). As indicated from studies with patients with Huntington's disease the basal ganglia have been found to be involved in disgust recognition also from vocal expressions (Sprenelmeyer et al., 1996; Speedie et al., 1990). Many of these implicated areas and their putative functional roles are consistent with previous findings provided from anatomic descriptions, animal experiments, and human lesion studies. However, the question of dissociable neuronal networks subserving distinct emotions is still debated and additional research is needed in order to fully understand the components of the neural systems and the exact mechanisms of emotional processing.

3. Objective

Dystonia is considered to manifest basically with pure motor deficit. However, evidence indicates that the motor disturbances in primary dystonia are accompanied

by cognitive impairments and psychiatric comorbidity. Despite the growing interest in the non-motor manifestations of dystonia, emotional communication processing is yet insufficiently investigated. Survey of the literature revealed only one study addressing the aspect of affective communication in dystonia patients while emotional processing in other basal ganglia disorders like Parkinson's (PD) and Huntington's (HD) diseases has been well studied. [Rinnerthaler et al. \(2006\)](#) point to a significantly impaired recognition of disgust from facial expressions in patients with primary cervical dystonia and blepharospasm. However, it remains unclear if affective speech recognition in dystonia patients is also affected. Primary cervical dystonia (CD) is the most frequent form of adult-onset focal dystonias with a prevalence 23-130 cases/1million ([Defazio et al., 2004, 2007](#)) and even though the underlying pathophysiologic mechanisms of the illness remain unclear it is considered to originate mainly from basal ganglia dysfunction. Based on the concept that basal ganglia are integrated into neural circuits subserving emotional prosody processing we hypothesized that alike other movement disorders patients with primary cervical dystonia would encounter difficulties in decoding the prosodic contours from affective speech. Moreover we sought to find out if a given deficit is restricted to specific emotional categories or if the affective speech recognition is generally affected. By using event related brain potentials, the present study aimed also to disclose the neurophysiological correlates of emotional processing in CD patients and disentangle the question whether potentially impaired affective prosody recognition in CD is constrained or not to a deficient processing of the valence or arousal affective dimension. Assuming the concept of [Posner et al \(2005\)](#) that the mesolimbic dopaminergic system might be responsible for processing of emotional valence and the reticular formation for emotional arousal, we hypothesised that CD patients will

demonstrate deficit in processing only the valence features of a vocal emotional message.

Furthermore, numerous studies suggest that primary dystonia is associated with a higher prevalence of psychiatric disorders, particularly anxiety and depression. However, so far no conclusive data exist to answer the question if depression, anxiety or specific personality traits correlate with deficits in recognition of emotional prosody or facial expressions. Therefore, another aspect of our study was to consider the psychological status and personality profile of CD patients and to determine possible correlations with the performance of emotional prosody recognition.

Hence, in the present study we aimed to address the following questions: 1) is primary cervical dystonia alike other movement disorders associated with a deficient processing of emotional prosody, 2) how these potential impairments are reflected by the elicited event related brain potentials 3) is the potential deficit restricted to specific emotional categories or the affective speech recognition is rather generally affected, 4) do the disturbances involve the processing of both valence and arousal features the emotional tone or are instead constrained to one of these affective dimensions and 5) are there any correlations between the psychopathological status and/or the psychological profile of CD patients with the emotional prosody recognition ratings.

References:

- Adolphs R. Neural systems for recognizing emotion. *Current opinion in neurobiology* 2002;12:169-177.
- Adolphs R, Gosselin F, Buchanan TW, Tranel D, Schyns P, Damasio AR. A mechanism for impaired fear recognition after amygdala damage. *Nature* 2005;433:68-72.
- Adolphs R, Tranel D. Intact recognition of emotional prosody following amygdala damage. *Neuropsychologia* 1999;37:1285-1292.
- Adolphs R, Tranel D, Damasio H, Damasio A. Impaired recognition of emotion in facial expressions following bilateral damage to the human amygdala. *Nature* 1994;372:669-672.
- Adolphs R, Tranel D, Damasio H, Damasio AR. Fear and the human amygdala. *J Neurosci* 1995;15:5879-5891.
- Anderson AK, Phelps EA. Intact recognition of vocal expressions of fear following bilateral lesions of the human amygdala. *Neuroreport* 1998;9:3607-3613.
- Ariatti A, Benuzzi F, Nichelli P. Recognition of emotions from visual and prosodic cues in Parkinson's disease. *Neurol Sci* 2008;29:219-227.
- Bach DR, Grandjean D, Sander D, Herdener M, Strik WK, Seifritz E. The effect of appraisal level on processing of emotional prosody in meaningless speech. *NeuroImage* 2008;42:919-927.
- Balas M, Peretz C, Badarny S, Scott RB, Giladi N. Neuropsychological profile of DYT1 dystonia. *Mov Disord* 2006;21:2073-2077.
- Banse R, Scherer KR. Acoustic profiles in vocal emotion expression. *Journal of personality and social psychology* 1996;70:614-636.
- Bard P. A diencephalic mechanism for the expression of rage with special reference to the central nervous system. *Am. J. Physiol.*, 84:490:513, 192. 1928.
- Belin P, Fecteau S, Bedard C. Thinking the voice: neural correlates of voice perception. *Trends in cognitive sciences* 2004;8:129-135.
- Benke T, Bosch S, Andree B. A study of emotional processing in Parkinson's disease. *Brain and cognition* 1998;38:36-52.
- Berardelli A, Rothwell JC, Hallett M, Thompson PD, Manfredi M, Marsden CD. The pathophysiology of primary dystonia. *Brain* 1998;121 (Pt 7):1195-1212.
- Black KJ, Ongur D, Perlmuter JS. Putamen volume in idiopathic focal dystonia. *Neurology* 1998;51:819-824.
- Blonder LX, Bowers D, Heilman KM. The role of the right hemisphere in emotional communication. *Brain* 1991;114 (Pt 3):1115-1127.
- Borod JC. Interhemispheric and intrahemispheric control of emotion: a focus on unilateral brain damage. *Journal of consulting and clinical psychology* 1992;60:339-348.
- Borod JC, Bloom RL, Brickman AM, Nakhutina L, Curko EA. Emotional processing deficits in individuals with unilateral brain damage. *Applied neuropsychology* 2002;9:23-36.
- Borod JC, Cicero BA, Obler LK, Welkowitz J, Erhan HM, Santschi C, Grunwald IS, Agosti RM, Whalen JR. Right hemisphere emotional perception: evidence across multiple channels. *Neuropsychology* 1998;12:446-458.
- Borod JC, Koff E, Lorch MP, Nicholas M. Channels of emotional expression in patients with unilateral brain damage. *Archives of neurology* 1985;42:345-348.

- Bowers D, Coslett HB, Bauer RM, Speedie LJ, Heilman KM. Comprehension of emotional prosody following unilateral hemispheric lesions: processing defect versus distraction defect. *Neuropsychologia* 1987;25:317-328.
- Brancati F, Defazio G, Caputo V, Valente EM, Pizzuti A, Livrea P, Berardelli A, D'Alapiccola B. Novel Italian family supports clinical and genetic heterogeneity of primary adult-onset torsion dystonia. *Mov Disord* 2002;17:392-397.
- Breitenstein C, Daum I, Ackermann H. Emotional processing following cortical and subcortical brain damage: contribution of the fronto-striatal circuitry. *Behavioural neurology* 1998;11:29-42.
- Breitenstein C, Van Lancker D, Daum I, Waters CH. Impaired perception of vocal emotions in Parkinson's disease: influence of speech time processing and executive functioning. *Brain and cognition* 2001;45:277-314.
- Breiter HC, Etcoff NL, Whalen PJ, Kennedy WA, Rauch SL, Buckner RL, Strauss MM, Hyman SE, Rosen BR. Response and habituation of the human amygdala during visual processing of facial expression. *Neuron* 1996;17:875-887.
- Bressman SB. Dystonia genotypes, phenotypes, and classification. *Advances in neurology* 2004;94:101-107.
- Broks P, Young AW, Maratos EJ, Coffey PJ, Calder AJ, Isaac CL, Mayes AR, Hodges JR, Montaldi D, Cezayirli E, Roberts N, Hadley D. Face processing impairments after encephalitis: amygdala damage and recognition of fear. *Neuropsychologia* 1998;36:59-70.
- Broocks A, Thiel A, Angerstein D, Dressler D. Higher prevalence of obsessive-compulsive symptoms in patients with blepharospasm than in patients with hemifacial spasm. *The American journal of psychiatry* 1998;155:555-557.
- Buchanan TW, Lutz K, Mirzazade S, Specht K, Shah NJ, Zilles K, Jancke L. Recognition of emotional prosody and verbal components of spoken language: an fMRI study. *Brain research* 2000;9:227-238.
- Bugalho P, Correa B, Guimaraes J, Xavier M. Obsessive-compulsive disorder and executive deficits in two patients with primary dystonia. *Parkinsonism & related disorders* 2006;12:388-391.
- Burke RE, Brin MF, Fahn S, Bressman SB, Moskowitz C. Analysis of the clinical course of non-Jewish, autosomal dominant torsion dystonia. *Mov Disord* 1986;1:163-178.
- Calder AJ, Keane J, Lawrence AD, Manes F. Impaired recognition of anger following damage to the ventral striatum. *Brain* 2004;127:1958-1969.
- Calder AJ, Young AW, Rowland D, Perrett DI, Hodges JR, Etcoff NL. Facial emotion recognition after bilateral amygdala damage: differentially severe impairment of fear. *Cogn Neuropsychol* ; 13: 699-745. 1996.
- Cancelliere AE, Kertesz A. Lesion localization in acquired deficits of emotional expression and comprehension. *Brain and cognition* 1990;13:133-147.
- Cannon WB. The James-Lange theory of emotions: a critical examination and an alternative theory. By Walter B. Cannon, 1927. *The American journal of psychology* 1987;100:567-586.
- Canli T, Desmond JE, Zhao Z, Glover G, Gabrieli JD. Hemispheric asymmetry for emotional stimuli detected with fMRI. *Neuroreport* 1998;9:3233-3239.
- Cavallaro R, Galardi G, Cavallini MC, Henin M, Amodio S, Bellodi L, Comi G. Obsessive compulsive disorder among idiopathic focal dystonia patients: an epidemiological and family study. *Biological psychiatry* 2002;52:356-361.
- Dara C, Monetta L, Pell MD. Vocal emotion processing in Parkinson's disease: reduced sensitivity to negative emotions. *Brain Res* 2008;1188:100-111.
- Darby DG. Sensory aprosodia: a clinical clue to lesions of the inferior division of the right middle cerebral artery? *Neurology* 1993;43:567-572.
- Darwin C. *The Expression of the Emotions in Man and Animals*, 1872. 1965.

- Davidson RJ. Cerebral asymmetries, emotion and affective style. In R. J. Davidson and K. Hugdahl (Eds.), *Brain asymmetry*, pp. 361-387; Cambridge MA: MIT Press 1995.
- Davidson RJ, Tomarken AJ. Laterality and emotion: An electrophysiological approach. In *Handbook of Neuropsychology*, F. Boller and J. Grafman, (Eds.), pp. 419-441. Elsevier, Amsterdam. 1989.
- De Carvalho Aguiar PM, Ozelius LJ. Classification and genetics of dystonia. *Lancet neurology* 2002;1:316-325.
- Defazio G, Abbruzzese G, Livrea P, Berardelli A. Epidemiology of primary dystonia. *Lancet neurology* 2004;3:673-678.
- Defazio G, Berardelli A, Hallett M. Do primary adult-onset focal dystonias share aetiological factors? *Brain* 2007;130:1183-1193.
- Defazio G, Brancati F, Valente EM, Caputo V, Pizzuti A, Martino D, Abbruzzese G, Livrea P, Berardelli A, Dallapiccola B. Familial blepharospasm is inherited as an autosomal dominant trait and relates to a novel unassigned gene. *Mov Disord* 2003;18:207-212.
- Draganski B, Thun-Hohenstein C, Bogdahn U, Winkler J, May A. "Motor circuit" gray matter changes in idiopathic cervical dystonia. *Neurology* 2003;61:1228-1231.
- Duane DD. Re: Executive cognitive deficits in primary dystonia. *Mov Disord* 2004;19:116-117; author reply 117.
- Duane DD, Vermilion KJ. Cognition and affect in patients with cervical dystonia with and without tremor. *Advances in neurology* 2004;94:179-189.
- Duane DD, Vermilion KJ. Cognitive deficits in patients with essential tremor. *Neurology* 2002;58:1706; author reply 1706.
- Eckman P, Friesen W, Ellsworth P. *Emotion in the Human Face: Guidelines for Research and an Integration of Findings*. Pergamon Press. 1972.
- Eidelberg D, Moeller JR, Ishikawa T, Dhawan V, Spetsieris P, Przedborski S, Fahn S. The metabolic topography of idiopathic torsion dystonia. *Brain* 1995;118 (Pt 6):1473-1484.
- Ekman P. An argument for basic emotions. *Cognition and Emotion*; 6:169-200. 1992.
- Ekman P. Basic Emotions. In T. Dalgleish & M. Power (Eds.), *Handbook of Cognition and Emotion* (pp. 45-60). Chichester: John Wiley and Sons Co. 1999.
- Ekman P. Cross-cultural studies of facial expression. In P. Ekman (Ed.), *Darwin and facial expression: A century of research in review* (pp. 169-222). New York: Academic Press. 1973.
- Ekman P, Friesen WV, O'Sullivan M, Chan A, Diacoyanni-Tarlatzis I, Heider K. Universals and cultural differences in the judgments of facial expressions of emotion. *Journal of Personality & Social Psychology*, 53(4), 712-717. *Expression of Anger across Cultures* 1987.
- Ekman P, Sorenson ER, Friesen WV. Pan-cultural elements in facial displays of emotion. *Science (New York, N.Y)* 1969;164:86-88.
- Esslen M, Pascual-Marqui RD, Hell D, Kochi K, Lehmann D. Brain areas and time course of emotional processing. *NeuroImage* 2004;21:1189-1203.
- Etgen T, Muhlau M, Gaser C, Sander D. Bilateral grey-matter increase in the putamen in primary blepharospasm. *Journal of neurology, neurosurgery, and psychiatry* 2006;77:1017-1020.
- Fahn S. Concept and classification of dystonia. *Advances in neurology* 1988;50:1-8.
- Fahn S, Bressman SB, Marsden CD. Classification of dystonia. *Advances in neurology* 1998;78:1-10.
- Furukawa Y, Rajput A, Nygaard T, Hornykiewicz O, Kish S. Biopterin biosynthetic abnormality in brains of genetically proven patients with hereditary progressive and Dopa-responsive dystonia. In: Fahn S, De Long M, Marsden CD, editors. *Dystonia 3. Advances in neurology*. Philadelphia: Lippincott-Raven. In press 1998. 1998.

- Gagnon L, Peretz I. Laterality effects in processing tonal and atonal melodies with affective and nonaffective task instructions. *Brain and cognition* 2000;43:206-210.
- Gainotti G. The meaning of emotional disturbances resulting from unilateral brain injury. In: *Emotions and the dual brain*, G. Gainotti and C. Caltagirone, (eds). Springer, Heidelberg; pp. 173–202. 1989.
- Galardi G, Perani D, Grassi F, Bressi S, Amadio S, Antoni M, Comi GC, Canal N, Fazio F. Basal ganglia and thalamo-cortical hypermetabolism in patients with spasmodic torticollis. *Acta neurologica Scandinavica* 1996;94:172-176.
- Garraux G, Bauer A, Hanakawa T, Wu T, Kansaku K, Hallett M. Changes in brain anatomy in focal hand dystonia. *Annals of neurology* 2004;55:736-739.
- George MS, Parekh PI, Rosinsky N, Ketter TA, Kimbrell TA, Heilman KM, Herscovitch P, Post RM. Understanding emotional prosody activates right hemisphere regions. *Archives of neurology* 1996;53:665-670.
- Goodglass H, Kaplan E. *The assessment of aphasia and related disorders*, Lea and Febinger, Philadelphia. 1983.
- Grandjean D, Sander D, Pourtois G, Schwartz S, Seghier ML, Scherer KR, Vuilleumier P. The voices of wrath: brain responses to angry prosody in meaningless speech. *Nature neuroscience* 2005;8:145-146.
- Gray JM, Young AW, Barker WA, Curtis A, Gibson D. Impaired recognition of disgust in Huntington's disease gene carriers. *Brain* 1997;120 (Pt 11):2029-2038.
- Greene P, Kang UJ, Fahn S. Spread of symptoms in idiopathic torsion dystonia. *Mov Disord* 1995;10:143-152.
- Grundmann K. Primary torsion dystonia. *Archives of neurology* 2005;62:682-685.
- Gundel H, Wolf A, Xidara V, Busch R, Ceballos-Baumann AO. Social phobia in spasmodic torticollis. *Journal of neurology, neurosurgery, and psychiatry* 2001;71:499-504.
- Gundel H, Wolf A, Xidara V, Busch R, Ladwig KH, Jacobi F, von Rad M, Ceballos-Baumann AO. High psychiatric comorbidity in spasmodic torticollis: a controlled study. *The Journal of nervous and mental disease* 2003;191:465-473.
- Heiman GA, Ottman R, Saunders-Pullman RJ, Ozelius LJ, Risch NJ, Bressman SB. Increased risk for recurrent major depression in DYT1 dystonia mutation carriers. *Neurology* 2004;63:631-637.
- Heiman GA, Ottman R, Saunders-Pullman RJ, Ozelius LJ, Risch NJ, Bressman SB. Obsessive-compulsive disorder is not a clinical manifestation of the DYT1 dystonia gene. *Am J Med Genet B Neuropsychiatr Genet* 2007;144B:361-364.
- Hierholzer J, Cordes M, Schelosky L, Richter W, Keske U, Venz S, Semmler W, Poewe W, Felix R. Dopamine D2 receptor imaging with iodine-123-iodobenzamide SPECT in idiopathic rotational torticollis. *J Nucl Med* 1994;35:1921-1927.
- Horstink CA, Praamstra P, Horstink MW, Berger HJ, Booij J, Van Royen EA. Low striatal D2 receptor binding as assessed by [¹²³I]IBZM SPECT in patients with writer's cramp. *Journal of neurology, neurosurgery, and psychiatry* 1997;62:672-673.
- Isenberg N, Silbersweig D, Engelen A, Emmerich S, Malavade K, Beattie B, Leon AC, Stern E. Linguistic threat activates the human amygdala. *Proceedings of the National Academy of Sciences of the United States of America* 1999;96:10456-10459.
- Izard CE. Four systems for emotion activation: Cognitive and noncognitive processes. *Psychological Review*, 100, 68–90.. 1993.
- Izard CE. *Human emotions*. New York: Plenum. 1977.
- Izard CE. Innate and universal facial expressions: evidence from developmental and cross-cultural research. *Personality: Critical Concepts in Psychology*, 115:288-99. 1998.
- Izard CE. Innate and universal facial expressions: Evidence from developmental and cross-cultural research. *Psychological Bulletin*, 115, 288–299. 1994

CAPTER 1

- Jabusch HC, Muller SV, Altenmuller E. Anxiety in musicians with focal dystonia and those with chronic pain. *Mov Disord* 2004;19:1169-1175.
- Jahanshahi M, Rowe J, Fuller R. Cognitive executive function in dystonia. *Mov Disord* 2003;18:1470-1481.
- James W. What is an emotion? *Mind*, 9(34):188-205, 1884.
- Kotz SA, Meyer M, Alter K, Besson M, von Cramon DY, Friederici AD. On the lateralization of emotional prosody: an event-related functional MR investigation. *Brain and language* 2003;86:366-376.
- Lang PJ, Bradley MM, Cuthbert BN. Emotion, motivation, and anxiety: brain mechanisms and psychophysiology. *Biological psychiatry* 1998;44:1248-1263.
- Lange C. *The Emotions*. Williams and Wilkins, Baltimore, Maryland, 1885.
- Larsen RJ, Diener E. Promises and problems with the circumplex model of emotion. In: Clark, MS (Ed.), *Review of personality and social psychology*. 13; Newbury Park, CA: Sage; p. 25-59. 1992.
- Lauterbach EC, Freeman A, Vogel RL. Differential DSM-III psychiatric disorder prevalence profiles in dystonia and Parkinson's disease. *The Journal of neuropsychiatry and clinical neurosciences* 2004;16:29-36.
- Lazarus D. *Emotion and adaptation*. New York: Oxford University Press. 1991.
- Lewis L, Butler A, Jahanshahi M. Depression in focal, segmental and generalized dystonia. *Journal of neurology* 2008;255:1750-1755.
- Liegeois-Chauvel C, Lorenzi C, Trebuchon A, Regis J, Chauvel P. Temporal envelope processing in the human left and right auditory cortices. *Cereb Cortex* 2004;14:731-740.
- Lloyd AJ. Comprehension of prosody in Parkinson's disease. *Cortex; a journal devoted to the study of the nervous system and behavior* 1999;35:389-402.
- Magyar-Lehmann S, Antonini A, Roelcke U, Maguire RP, Missimer J, Meyer M, Leenders KL. Cerebral glucose metabolism in patients with spasmodic torticollis. *Mov Disord* 1997;12:704-708.
- Marsden CD, Harrison MJ, Bunday S. Natural history of idiopathic torsion dystonia. *Advances in neurology* 1976;14:177-187.
- Marsden CD, Obeso JA, Zarranz JJ, Lang AE. The anatomical basis of symptomatic hemidystonia. *Brain* 1985;108 (Pt 2):463-483.
- Miller KM, Okun MS, Fernandez HF, Jacobson CE, Rodriguez RL, Bowers D. Depression symptoms in movement disorders: comparing Parkinson's disease, dystonia, and essential tremor. *Mov Disord* 2007;22:666-672.
- Mitchell RL. How does the brain mediate interpretation of incongruent auditory emotions? The neural response to prosody in the presence of conflicting lexico-semantic cues. *The European journal of neuroscience* 2006;24:3611-3618.
- Mitchell RL, Elliott R, Barry M, Cruttenden A, Woodruff PW. The neural response to emotional prosody, as revealed by functional magnetic resonance imaging. *Neuropsychologia* 2003;41:1410-1421.
- Moraru E, Schnider P, Wimmer A, Wenzel T, Birner P, Griengl H, Auff E. Relation between depression and anxiety in dystonic patients: implications for clinical management. *Depression and anxiety* 2002;16:100-103.
- Morris JS, Frith CD, Perrett DI, Rowland D, Young AW, Calder AJ, Dolan RJ. A differential neural response in the human amygdala to fearful and happy facial expressions. *Nature* 1996;383:812-815.
- Morris JS, Scott SK, Dolan RJ. Saying it with feeling: neural responses to emotional vocalizations. *Neuropsychologia* 1999;37:1155-1163.
- Muller J, Kemmler G, Wissel J, Schneider A, Voller B, Grossmann J, Diez J, Homann N, Wenning GK, Schnider P, Poewe W. The impact of blepharospasm and cervical dystonia on health-related quality of life and depression. *Journal of neurology* 2002;249:842-846.

- Naumann M, Pirker W, Reiners K, Lange KW, Becker G, Brucke T. Imaging the pre- and postsynaptic side of striatal dopaminergic synapses in idiopathic cervical dystonia: a SPECT study using [123I] epidepride and [123I] beta-CIT. *Mov Disord* 1998;13:319-323.
- Otsuka M, Ichiya Y, Shima F, Kuwabara Y, Sasaki M, Fukumura T, Kato M, Masuda K, Goto I. Increased striatal 18F-dopa uptake and normal glucose metabolism in idiopathic dystonia syndrome. *Journal of the neurological sciences* 1992;111:195-199.
- Ozel-Kizil ET, Akbostanci MC, Ozguven HD, Atbasoglu EC. Secondary social anxiety in hyperkinesias. *Mov Disord* 2008;23:641-645.
- Ozelius LJ, Hewett JW, Page CE, Bressman SB, Kramer PL, Shalish C, de Leon D, Brin MF, Raymond D, Corey DP, Fahn S, Risch NJ, Buckler AJ, Gusella JF, Breakefield XO. The early-onset torsion dystonia gene (DYT1) encodes an ATP-binding protein. *Nature genetics* 1997;17:40-48.
- Panksepp J. *Affective neuroscience: The foundations of human and animal emotions*. New York: Oxford University Press. 1998.
- Parker GJ, Luzzi S, Alexander DC, Wheeler-Kingshott CA, Ciccarelli O, Lambon Ralph MA. Lateralization of ventral and dorsal auditory-language pathways in the human brain. *NeuroImage* 2005;24:656-666.
- Paulmann S, Pell MD, Kotz SA. Functional contributions of the basal ganglia to emotional prosody: evidence from ERPs. *Brain Res* 2008;1217:171-178.
- Pauls DL, Korczyn AD. Complex segregation analysis of dystonia pedigrees suggests autosomal dominant inheritance. *Neurology* 1990;40:1107-1110.
- Pell MD. Cerebral mechanisms for understanding emotional prosody in speech. *Brain and language* 2006;96:221-234.
- Pell MD. On the receptive prosodic loss in Parkinson's disease. *Cortex; a journal devoted to the study of the nervous system and behavior* 1996;32:693-704.
- Pell MD. Recognition of prosody following unilateral brain lesion: influence of functional and structural attributes of prosodic contours. *Neuropsychologia* 1998;36:701-715.
- Pell MD, Leonard CL. Processing emotional tone from speech in Parkinson's disease: a role for the basal ganglia. *Cognitive, affective & behavioral neuroscience* 2003;3:275-288.
- Peller M, Zeuner KE, Munchau A, Quartarone A, Weiss M, Knutzen A, Hallett M, Deuschl G, Siebner HR. The basal ganglia are hyperactive during the discrimination of tactile stimuli in writer's cramp. *Brain* 2006;129:2697-2708.
- Peretz I, Kolinsky R, Tramo M, Labrecque R, Huble C, Demeurisse G, Belleville S. Functional dissociations following bilateral lesions of auditory cortex. *Brain* 1994;117 (Pt 6):1283-1301.
- Perlmutter JS, Stambuk MK, Markham J, Black KJ, McGee-Minnich L, Jankovic J, Moerlein SM. Decreased [18F]spiperone binding in putamen in idiopathic focal dystonia. *J Neurosci* 1997;17:843-850.
- Pettigrew LC, Jankovic J. Hemidystonia: a report of 22 patients and a review of the literature. *Journal of neurology, neurosurgery, and psychiatry* 1985;48:650-657.
- Phan KL, Wager T, Taylor SF, Liberzon I. Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. *NeuroImage* 2002;16:331-348.
- Phillips ML, Young AW, Scott SK, Calder AJ, Andrew C, Giampietro V, Williams SC, Bullmore ET, Brammer M, Gray JA. Neural responses to facial and vocal expressions of fear and disgust. *Proceedings* 1998;265:1809-1817.
- Phillips ML, Young AW, Senior C, Brammer M, Andrew C, Calder AJ, Bullmore ET, Perrett DI, Rowland D, Williams SC, Gray JA, David AS. A specific neural substrate for perceiving facial expressions of disgust. *Nature* 1997;389:495-498.
- Pihan H, Altenmuller E, Ackermann H. The cortical processing of perceived emotion: a DC-potential study on affective speech prosody. *Neuroreport* 1997;8:623-627.

- Pihan H, Altenmuller E, Hertrich I, Ackermann H. Cortical activation patterns of affective speech processing depend on concurrent demands on the subvocal rehearsal system. A DC-potential study. *Brain* 2000;123 (Pt 11):2338-2349.
- Playford ED, Fletcher NA, Sawle GV, Marsden CD, Brooks DJ. Striatal [18F]dopa uptake in familial idiopathic dystonia. *Brain* 1993;116 (Pt 5):1191-1199.
- Plutchik R. Emotions: A general psychoevolutionary theory. In Scherer K.R. and Ekman (Eds.), *Approaches to Emotion*, pp197-219. 1984.
- Plutchik R. A general psychoevolutionary theory of emotion. In R. Plutchik and H. Kellerman (Eds.), *Emotion: Theory, research, and experience: Vol. 1. Theories of emotion* (pp. 3–33). New York: Academic Press. 1980.
- Posner J, Russell JA, Peterson BS. The circumplex model of affect: an integrative approach to affective neuroscience, cognitive development, and psychopathology. *Development and psychopathology* 2005;17:715-734.
- Rinnerthaler M, Benecke C, Bartha L, Entner T, Poewe W, Mueller J. Facial recognition in primary focal dystonia. *Mov Disord* 2006;21:78-82.
- Ross ED. The aprosodias. Functional-anatomic organization of the affective components of language in the right hemisphere. *Archives of neurology* 1981;38:561-569.
- Ross ED, Monnot M. Neurology of affective prosody and its functional-anatomic organization in right hemisphere. *Brain and language* 2008;104:51-74.
- Ross ED, Thompson RD, Yenkosky J. Lateralization of affective prosody in brain and the callosal integration of hemispheric language functions. *Brain and language* 1997;56:27-54.
- Russell JA. A circumplex model of affect. *Journal of Personality and Social Psychology* 1980;39.
- Russell JA, Fehr B. Fuzzy concepts in a fuzzy hierarchy: Varieties of anger. *Journal of Personality and Social Psychology*; 67:186–205. 1994.
- Saunders-Pullman R, Shriberg J, Heiman G, Raymond D, Wendt K, Kramer P, Schilling K, Kurlan R, Klein C, Ozelius LJ, Risch NJ, Bressman SB. Myoclonus dystonia: possible association with obsessive-compulsive disorder and alcohol dependence. *Neurology* 2002;58:242-245.
- Schachter S, Singer JE. Cognitive, Social, and Physiological Determinants of Emotional State. *Psychological Review*, 69(5), 379-399. . 1962.
- Scherer KR. Physiological models of emotion. In J.C. Borod (Ed.), *The neurophysiology of emotion*, pp.137-162; New York: Oxford University Press. 2000.
- Schirmer A, Kotz SA. Beyond the right hemisphere: brain mechanisms mediating vocal emotional processing. *Trends in cognitive sciences* 2006;10:24-30.
- Schroder C, Mobes J, Schutze M, Szymanowski F, Nager W, Bangert M, Munte TF, Dengler R. Perception of emotional speech in Parkinson's disease. *Mov Disord* 2006;21:1774-1778.
- Scott RB, Gregory R, Wilson J, Banks S, Turner A, Parkin S, Giladi N, Joint C, Aziz T. Executive cognitive deficits in primary dystonia. *Mov Disord* 2003;18:539-550.
- Scott SK, Young AW, Calder AJ, Hellawell DJ, Aggleton JP, Johnson M. Impaired auditory recognition of fear and anger following bilateral amygdala lesions. *Nature* 1997;385:254-257.
- Silberman EK, Weingartner H. Hemispheric lateralization of functions related to emotion. *Brain and cognition* 1986;5:322-353.
- Speedie LJ, Brake N, Folstein SE, Bowers D, Heilman KM. Comprehension of prosody in Huntington's disease. *Journal of neurology, neurosurgery, and psychiatry* 1990;53:607-610.
- Sprenghelmeyer R, Rausch M, Eysel UT, Przuntek H. Neural structures associated with recognition of facial expressions of basic emotions. *Proceedings* 1998;265:1927-1931.
- Sprenghelmeyer R, Young AW, Calder AJ, Karnat A, Lange H, Homborg V, Perrett DI, Rowland D. Loss of disgust. Perception of faces and emotions in Huntington's disease. *Brain* 1996;119 (Pt 5):1647-1665.

- Starkstein SE, Federoff JP, Price TR, Leiguarda RC, Robinson RG. Neuropsychological and neuroradiologic correlates of emotional prosody comprehension. *Neurology* 1994;44:515-522.
- Stone VE, Nisenson L, Eliassen JC, Gazzaniga MS. Left hemisphere representations of emotional facial expressions. *Neuropsychologia* 1996;34:23-29.
- Suzuki A, Hoshino T, Shigemasu K, Kawamura M. Disgust-specific impairment of facial expression recognition in Parkinson's disease. *Brain* 2006;129:707-717
- Tarsy D, Simon DK. Dystonia. *The New England journal of medicine* 2006;355:818-829.
- Thayer RE. *The origin of everyday moods: Managing energy, tension and stress*. New York: Oxford University Press. 1989.
- Tomkins S. *Affect, imagery, consciousness; Vol. 1: The positive affect*; New York: Springer. 1962.
- Tomkins SS. Affect theory. In K.R. Scherer and P. Eckman (Eds.), *Approaches to emotion*; pp.163-196. Hillsdale, NJ: Erlbaum. 1984.
- Tomkins SS. *Affect, imagery, consciousness; Vol. 2: The negative affect*; New York: Springer. 1963.
- Van Lancker D, Sidtis JJ. The identification of affective-prosodic stimuli by left- and right-hemisphere-damaged subjects: all errors are not created equal. *Journal of speech and hearing research* 1992;35:963-970.
- Wambacq IJ, Jerger JF. Processing of affective prosody and lexical-semantics in spoken utterances as differentiated by event-related potentials. *Brain research* 2004;20:427-437.
- Watson D, Clark LA. On traits and temperament: General and specific factors of emotional experience and their relation to the five-factor model. *Journal of Personality*; 60:441-475. 1992.
- Weddell RA. Recognition memory for emotional facial expressions in patients with focal cerebral lesions. *Brain and cognition* 1989;11:1-17.
- Wenzel T, Schnider P, Wimmer A, Steinhoff N, Moraru E, Auff E. Psychiatric comorbidity in patients with spasmodic torticollis. *Journal of psychosomatic research* 1998;44:687-690.
- Whalen PJ, Rauch SL, Etcoff NL, McInerney SC, Lee MB, Jenike MA. Masked presentations of emotional facial expressions modulate amygdala activity without explicit knowledge. *J Neurosci* 1998;18:411-418.
- Wildgruber D, Hertrich I, Riecker A, Erb M, Anders S, Grodd W, Ackermann H. Distinct frontal regions subserved evaluation of linguistic and emotional aspects of speech intonation. *Cereb Cortex* 2004;14:1384-1389.
- Wildgruber D, Pihan H, Ackermann H, Erb M, Grodd W. Dynamic brain activation during processing of emotional intonation: influence of acoustic parameters, emotional valence, and sex. *NeuroImage* 2002;15:856-869.
- Wildgruber D, Riecker A, Hertrich I, Erb M, Grodd W, Ethofer T, Ackermann H. Identification of emotional intonation evaluated by fMRI. *NeuroImage* 2005;24:1233-1241.
- Yip JT, Lee TM, Ho SL, Tsang KL, Li LS. Emotion recognition in patients with idiopathic Parkinson's disease. *Mov Disord* 2003;18:1115-1122.
- Yip JT, Leung KK, Li LS, Lee TM. The role of sub-cortical brain structures in emotion recognition. *Brain Inj* 2004;18:1209-1217.
- Zatorre RJ, Belin P. Spectral and temporal processing in human auditory cortex. *Cereb Cortex* 2001;11:946-953.
- Zeman W, Dyken P. Dystonia musculorum deformans. Clinical, genetic and pathoanatomical studies. *Psychiatria, neurologia, neurochirurgia* 1967;70:77-121.

Deficient Recognition of Emotional Prosody in Primary Focal Dystonia

1.1 Abstract

Primary dystonia is a central movement disorder attributed mainly to basal ganglia dysfunction. Besides motor control, striatopallidal structures are known to implement non-motor functions including processing of cognitive and emotional information. Previous research has already demonstrated deficient recognition of emotional faces in patients with primary focal dystonia. In the present study, 30 patients with primary cervical dystonia (CD) and 30 healthy control subjects (HC) had to classify auditory presented words according to their emotional prosody (angry, happy, relaxed, sad). Analysis of hit rates and reaction times revealed a significantly poorer performance of CD patients in judging angrily intonated words. Additional psychological assessment (SCL-90 R) demonstrated a higher level of psychological distress in CD patients who predominantly displayed symptoms of somatization, anxiety and depression. Moreover, dystonic patients showed accentuated personality features (FPI) regarding strain, somatic complaints and emotionality dimensions. Together these findings in CD patients highlight first the involvement of basal ganglia in emotional prosody recognition and second the importance to identify the psychopathological symptomatology in patients with cervical dystonia as complementary to the motor deficit.

1.2 Introduction

Primary dystonia is a central movement disorder (Fahn, 1988) considered to manifest mainly with pure motor deficit. However, evidence indicates that the typical motor disturbances are frequently accompanied by concomitant psychopathological symptoms (Miller et al., 2007; Lauterbach et al., 2004; Gundel et al., 2003; Jabusch et al., 2004; Moraru et al., 2002). Even though the exact pathophysiology of dystonia has still to be determined, it is associated mainly with basal ganglia dysfunction (Defazio et al., 2007; Berardelli et al., 1998). Besides their prominent role in the motor control, the striatopallidal structures are known to implement also non-motor functions such as processing of cognitive and emotional information (Alexander et al., 1990). Accumulating findings suggest that the basal ganglia and in particular the orbitofrontal loop play an essential role in affective speech comprehension (Paulmann et al., 2008; Pell and Leonard, 2003; Pell, 2002; Breitenstein et al., 1998). Such notion correlates with recent neuroimaging studies demonstrating bilateral involvement of putamen and caudate nucleus (Kotz et al., 2003) as well as pallidum and anterior insula (Wildgruber et al., 2002) in the perception of emotional prosody. Moreover, Bach and colleagues (Bach et al., 2008) propose that different appraisal levels of emotional prosody processing are subserved by amygdala-prefrontal-cingulate network and that structures like the anterior cingulate gyrus and the basal ganglia implement a specific role in the explicit emotional prosody identification. Rinnerthaler and colleagues (Rinnerthaler et al., 2006) have observed a significantly impaired performance of patients with cervical dystonia (CD) and blepharospasm in recognizing facial expressions of disgust. However, it remains unclear if the recognition of emotional speech in primary dystonia is also affected. Deficits of vocal emotional

communication have been reported in other movement disorders such as Parkinson's (Dara et al., 2008; Schroder et al., 2006; Yip et al., 2003; Breitenstein et al., 2001; Pell, 1996) and Huntington's diseases (Speedie et al., 1990; Sprengelmeyer et al., 1996). In a previous study we found a deficient perception of happily and sadly spoken words in Parkinson's disease patients as indicated by the behavioral and neurophysiological data (Schroder et al., 2006). The present study aimed first to address the question whether primary cervical dystonia, alike other movement disorders, is associated with a deficient processing of emotional prosody and second to find out if a potential deficit is restricted to selected emotional categories or the affective speech recognition is generally affected. Based on the aforementioned findings we hypothesized that patients with CD will display deficit in the emotional speech recognition.

Furthermore, the concomitance of mood disorders is one possible and often discussed confound when investigating emotional processing in patients with movement disorders. A number of complementary studies suggest that primary dystonia is associated with a higher prevalence of psychiatric disorders (Miller et al., 2007; Lauterbach et al., 2004; Gundel et al., 2003; Jabusch et al., 2004; Moraru et al., 2002), particularly anxiety and depression. However, so far no conclusive data exist to answer the question if depression, anxiety or specific personality traits correlate with deficits in recognition of emotional prosody or facial expressions. Therefore, an additional aspect of our study was to consider the psychological status and personality profile of CD patients and to determine possible correlations with the performance of emotional prosody recognition.

1.3 Subjects and Methods

Patients with primary cervical dystonia (CD, n=30) and healthy control subjects (HC, n=30) matched for age, gender and educational level participated in the experiment. The demographic and clinical data are presented in Table 1. To exclude dementia or clinical depression, only subjects scoring 28 or higher on the Mini-mental state examination (MMSE) and 18 or lower on the Beck Depression Inventory (BDI) were recruited. Each patient was classified according to the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) (Consky and Lang, 1994) and only those with mild to moderate primary cervical dystonia (TWSTRS, $M = 23.4 \pm 10.6$) participated in the study. All CD patients were on a regular treatment with botulinum toxin injections every three months and were investigated within two weeks before the next treatment session. Three of them additionally took tricyclic antidepressants, two benzodiazepines and one was receiving an anticholinergic medication.

None of the subjects had hearing impairments, hearing aids, otolaryngological, psychiatric or any other neurological diseases.

The study was approved by the local ethics committee and all participants gave written informed consent.

Table 1: Demographic and clinical data

	HC	CD
Sample size, n	30	30
Age, yr	56.6 (8.9)	56.7 (9.0)
Female/ male	16/14	16/14
Formal education, yr	12.3 (2.4)	10.8 (1.9)
MMSE score	29.5 (0.6)	29.1 (0.8)
BDI score	4.1 (4.7)*	8.3 (4.8)*
TWSTRS score	na	23.4 (10.6)
Duration of disease, yr	na	11.2 (8.9)
Age of disease onset, yr	na	45.0 (12.9)

Data presented as mean values (SD). CD, Cervical dystonia; HC, healthy controls; MMSE, Mini-Mental State Examination; BDI, Beck Depression Inventory; TWSTRS, Toronto Western Spasmodic Torticollis Rating Scale; * $p < 0.01$.

1.4 Stimuli and experimental design

Thirteen two-syllable words with semantically neutral content, spoken by experienced professional actors in four different emotional tones (angry, happy, relaxed and sad) were pre-recorded at AD conversion rate of 44 kHz. As described by GoydkeGoydke et al. , 2004 all stimuli were assessed by 23 naïve listeners and only those eliciting consistent evaluation were used for the experiment. The emotionally intoned words were arranged in a modified oddball (context violation) paradigm and played in a pseudo-random order with a probability of 0.8 for the frequent standard stimuli and of 0.2 for the rare deviants. A total of 800 words were presented in four blocks. Each block comprised 200 words including 40 deviants. According to Russell’s “Circumplex model of affect” (Russell, 1980) all emotions can be interpreted as a combination of varying degrees of *valence* (pleasure–displeasure) and *arousal* (high-low) dimensions. The study involved two experimental conditions. In *valence condition* the participants

were asked to rate the emotional prosody of each presented word, as positive or negative and in *arousal condition* as excited or calm respectively, by pressing one of three keyboard buttons with a third possible response “I do not know”. Each subject participated in one of the two experimental conditions as the subgroups were matched for age, gender and educational level. There was no significant difference for BDI and MMSE scores, as well as for CD duration, age of onset and TWSTRS score between the two subgroups.

Response latencies were measured from sound onset with the time-out point (time after which responses were registered as missing) set at 2500 ms. Reaction times and proportions of correct answers were obtained.

1.5 Psychological status and Personality profile

Additionally, all participants underwent a psychological assessment using two self-report questionnaires: Symptom Check List - 90 - Revised (SCL-90-R) Derogatis, 1977; Franke, and Freiburg Personality Inventory (FPI-R) (Fahrenberg et al., 2001). The SCL-90-R is a widely used instrument for psychopathological screening. It is interpreted in terms of nine primary symptom dimensions: somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism. In addition, three global indices of distress are reported: global severity index (GSI) indicating the overall level of psychological distress, positive symptom distress index (PSDI) - a measure for the intensity of the experienced symptoms and positive symptom total (PST), representing the number of the reported positive symptoms. The FPI-R (Fahrenberg et al., 2001) is a German inventory used for evaluation of key personality features and is interpreted in terms of

12 bipolar subscales: life satisfaction, social orientation, achievement orientation, inhibitedness, irritability, aggressiveness, strain, somatic complaints, health concern, frankness, extraversion and emotionality.

1.6 Statistical evaluation

Data were tested for normal distribution with Kolmogorov-Smirnov test. For comparison between CD and HC group, Student's t - test for independent samples (two tailed) and Mann-Whitney U test (two tailed) were implemented for the parametric and non-parametric data respectively. Linear Pearson's rho analysis was performed for additional correlations. P values of <0.05 were considered significant.

1.7 Results

The overall performance of CD patients in recognition of angry prosody was significantly poorer as compared to the HC group (Fig. 1). Proportions of correct responses to angry standards in CD patients (Mean, $M = 0.54$) were significantly lower than in HC ($M = 0.72$, $p=0.008$). Similar results were obtained for the responses to angry deviants (CD, $M = 0.63$; HC, $M = 0.80$; $p = 0.022$). The overall correct judgments of happy, relaxed and sad emotions did not reach significant levels between groups, neither for the standard nor for the deviant stimuli (Table 2). Additionally, responses of both groups for valence and arousal conditions were evaluated separately. The results of valence recognition task paralleled those of the overall emotion recognition. The dystonic patients performed inferiorly only in judging angry prosody, again for both standards (CD, $M = 0.41$; HC, $M = 0.65$; $p = 0.013$) and deviants (CD, $M = 0.44$; HC, $M = 0.77$; $p = 0.001$). In contrast, for the arousal

condition, there were no significant differences observed between both groups for any of the four emotions (Table 2).

Furthermore, reaction times of all responses were analyzed (Table 3). Interestingly and in consistence with the hit rates, the only significant group difference was obtained for angrily intonated words with slower responses of CD patients (CD, M = 1070 ms; HC, M = 947 ms; $p = 0.035$).

Table 2 Behavioral data of CD and HC

	<i>Emotion (n=30)</i>			<i>Valence (n=17)</i>			<i>Arousal (n=13)</i>		
	HC	CD	P	HC	CD	P	HC	CD	P
angry - std	0.71 (0.24)	0.54	0.008 **	0.65	0.41	0.013 *	0.81	0.70	0.159
happy -	0.56 (0.28)	0.48	0.278	0.63	0.53	0.325	0.48	0.42	0.603
relaxed -	0.44 (0.28)	0.41	0.658	0.27	0.25	0.700	0.65	0.61	0.639
sad -std	0.47 (0.34)	0.43	0.645	0.23	0.19	0.484	0.78	0.74	0.644
angry -	0.80 (0.21)	0.63	0.022 *	0.77	0.44	0.001 **	0.85	0.89	0.654
happy -	0.63 (0.26)	0.56	0.303	0.66	0.56	0.299	0.60	0.56	0.717
relaxed -	0.47 (0.33)	0.45	0.862	0.23	0.27	0.495	0.77	0.69	0.396
sad - dev	0.42 (0.37)	0.47	0.638	0.14	0.18	0.570	0.79	0.85	0.407

Behavioral data presented as mean (SD) proportions of correct responses (hits); CD, cervical dystonia; HC, healthy controls; std, standard (frequent) stimuli; dev, deviant (rare) stimuli. Note the significant difference for angry stimuli for both tasks together (*emotion*) and for the *valence* but not for the *arousal* condition (* $p < 0.05$, ** $p < 0.01$).

Table 3 Reaction times shown for CD and HC group

N =30	<i>Standards</i>				<i>Deviants</i>			
	angry	happy	relaxed	sad	angry	happy	relaxed	sad
HC	947 (212) *	1043 (246)	1221 (229)	1103 (279)	985 (213)	1045 (240)	1243 (257)	1129 (243)
CD	1070 (208) *	1161 (271)	1310 (257)	1179 (232)	1037 (236)	1134 (260)	1291(231)	1213 (288)

Data presented as mean values (SD). CD, cervical dystonia; HC, healthy controls. Reaction times (ms) measured from sound onset. Significant difference between CD and HC for angry standards, $P < 0.05$.

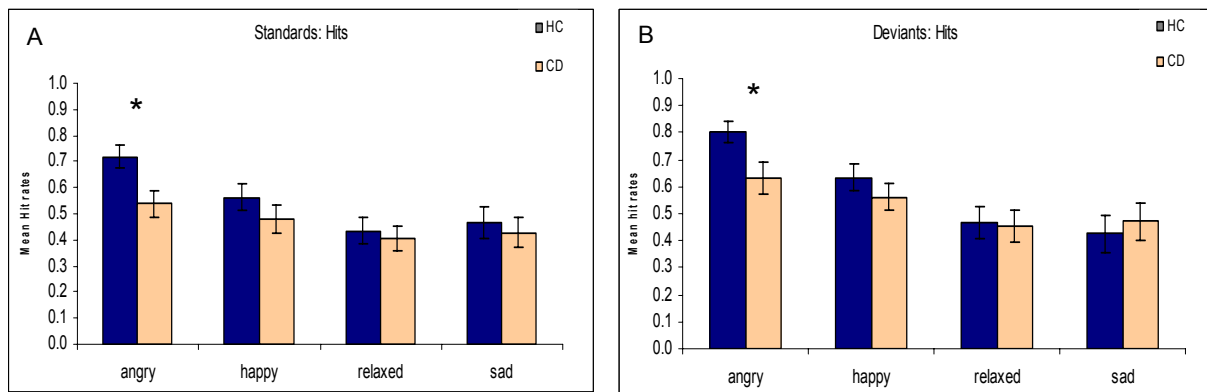


Fig.1 Behavioral data of CD, cervical dystonia (n=30) and HC, healthy controls (n=30); Data presented as mean (SD) proportions of correct (hits) responses for A. standard (frequent) stimuli and B. deviant (rare) stimuli; *P < 0.05, **P < 0.01.

Psychological status and Personality profile

The evaluation of self-reported psychological symptoms using SCL-90-R (Fig. 2) revealed a higher level of psychological distress in the CD group as indicated by GSI (CD, M = 53.63; HC, M = 44.97; $p = 0.005$). In addition, dystonic patients responded more often positively to the listed symptoms (CD, M = 53.90; HC, M = 46.40; $p = 0.016$). The intensity of the experienced symptoms in CD was also higher than in HC (CD, M = 51.17; HC, M = 45.80; $p = 0.022$). Moreover, the patient group displayed significantly elevated scores on seven out of nine primary symptom dimensions, namely: somatization (CD, M = 52.30; HC, M = 43.47; $p = 0.001$), obsessive-compulsive (CD, M = 53.63; HC, M = 47.43; $p = 0.041$), interpersonal sensitivity (CD, M = 55.27; HC, M = 49.77; $p = 0.039$), anxiety (CD, M = 53.60; HC, M = 47.23; $p = 0.020$), depression (CD, M = 53.53; HC, M = 47.97; $p = 0.048$), hostility (CD, M = 52.23; HC, M = 47.37; $p = 0.038$) and psychoticism (CD, M = 52.90; HC, M = 48.73; $p = 0.044$). There was no significant difference for phobic anxiety ($p = 0.583$) and paranoia ($p = 0.103$) dimensions.

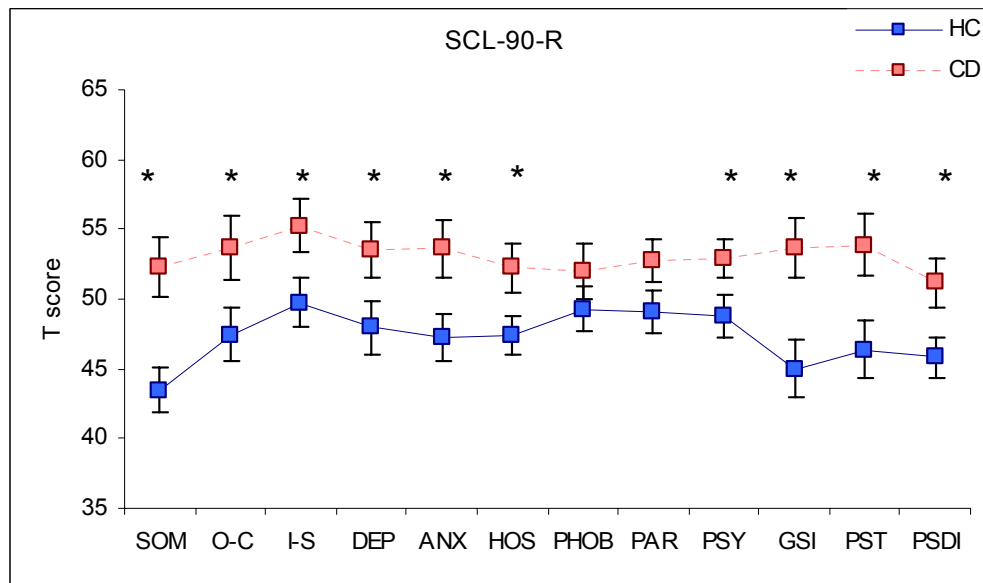


Fig.2 SCL-90-R clinical profile of CD, cervical dystonia and HC, healthy controls. Data presented as mean T scores; Error bars are SE; Significant difference between CD (n=30) and HC (n=30) for somatization (SOM), obsessive-compulsive (O-C), I-S (interpersonal sensitivity), depression (DEP), anxiety (ANX), hostility (HOS), psychoticism (PSY), global severity index (GSI), positive symptoms total (PST) and positive symptoms distress index PSDI; phobic anxiety (PHOB), paranoia (PAR); *P < 0.05, **P < 0.01.

Evaluation of the FPI-R profile (Fig. 3) was performed on 30 HC and 29 CD participants as one CD patient missed to fill out more than 7 items, preventing further test interpretations (Fahrenberg et al., 2001). Patients with CD showed significantly elevated stanine scores of strain (CD, M = 5.38; HC, M = 4.10; $p = 0.010$), somatic complaints (CD, M = 5.24; HC, M = 4.07; $p = 0.017$) and emotionality dimensions (CD, M = 5.41; HC, M = 4.27; $p = 0.046$) as well as lower scores of extroversion traits (CD, M = 4.03; HC, M = 5.17; $p = 0.025$). The rest of the personality subscales did not display any significant differences between both groups. Even though participants with BDI scores indicating clinically evident depression were excluded, statistical analysis revealed significant group difference (see Table 1) with higher BDI scores in CD patients (CD, M = 8.31; HC, M = 4.23; $p = 0.001$).

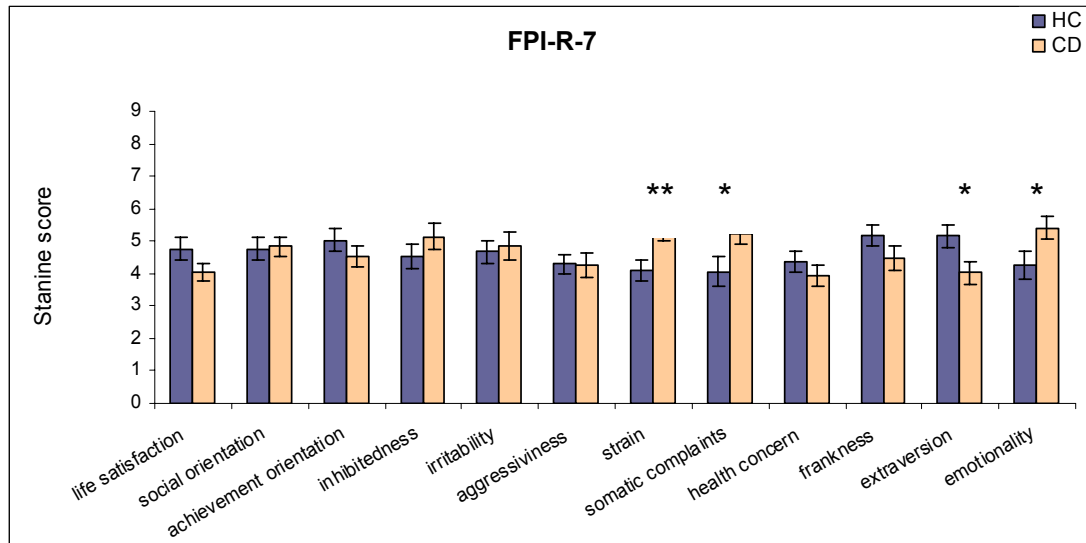


Fig.3 FPI-R personality profile of CD, cervical dystonia and HC, healthy control group. Data are presented as mean stanine scores; Error bars represent SE; Significant difference between CD (n=29) and HC (n=30) for strain, somatic complains, extraversion and emotionality; *P <0.05, ** P ≤ 0.01.

Additionally, no significant correlations were found between BDI, SCL-90-R- and FPI-R variables and the performance of emotional prosody recognition. Moreover, in CD patients, the ratings of angry prosody itself did not correlate with the disease severity, duration and age of onset.

1.8 Discussion

To our knowledge this study is the first that addresses the processing of emotional prosody information in patients with primary dystonia. The main finding of the present work discloses a significantly poorer performance of CD patients in rating angrily intonated words as compared to HC subjects. Correspondingly, the reaction times to angry stimuli were significantly slower in the CD group. Thus, in agreement with our hypothesis these results imply a deficient processing of emotional prosody in patients with primary cervical dystonia. Therefore, it appears that not only the recognition of

emotional facial expressions ([Rinnerthaler et al., 2006](#)) but also the perception of affective speech in CD might be affected.

Hence, the question arises how changes of emotional prosody processing can be explained in a disorder which is normally manifested with pure motor deficit. Even though the exact pathophysiology of primary dystonia remains unclear, it is attributed mainly to basal ganglia dysfunction and more specifically to overactivity of the direct striatopallidal pathway resulting in reduced globus pallidus internus output ([Berardelli et al., 1998](#); [Defazio et al., 2007](#)). Besides the prominent sensorimotor function, the basal ganglia are known to be additionally involved in distinct non-motor processes such as emotional-motivational and cognitive operations ([Alexander et al., 1990](#)). Moreover, converging evidence from studies with Parkinson's disease patients ([Pell and Leonard, 2003](#); [Breitenstein et al., 1998](#)), subcortical brain damage ([Paulmann et al., 2008](#)) and healthy subjects ([Kotz et al., 2003](#); [Wildgruber et al., 2002](#); [Bach et al., 2008](#)) suggest that striatopallidal structures play a crucial role in emotional prosody processing.

It is important to note that the present study demonstrated a deficit only for the recognition of angrily intonated words in CD patients. Generally, it appears that in basal ganglia disorders mainly the processing of emotions with negative connotation is disturbed. As cited above, individuals with CD and blepharospasm demonstrate a deficient decoding of disgust from facial expressions. By using fMRI [Calder and colleagues \(Calder et al., 2004\)](#) found that patients with lesions restricted to the ventral striatum display a disproportionate deficit in recognition of anger from facial and vocal expressions in contrast to the control group with more dorsally located lesions of the basal ganglia. Furthermore, [Johnson and colleagues \(Johnson et al., 2007\)](#) reported significantly less accurate recognition of negative

emotions (anger, disgust, fear, sadness) in Huntington's disease gen carriers. Likewise, several studies point to a deficient perception of emotional prosody with mainly negative connotation in patients with Parkinson's disease (Dara et al., 2008; Pell et al. , 2006; Yip et al., 2003). However, assuming the concept of dissociable neuronal systems responsible for negative/ positive emotions processing (Sprengelmeyer et al., 1998), CD patients should have displayed deficits also in rating sadly intonated words. Hence, our findings appear to comply rather with the idea that separate neuronal networks are accounted for the recognition of individual emotions (Sprengelmeyer et al., 1998; Blair et al. , 1999). Moreover, our results reveal a significant difference between CD and HC for emotional prosody ratings only in the valence but not the arousal condition. A similar dissociation has been reported by Dara and colleagues¹⁴ in patients with Parkinson's disease. Posner and co-authors (Posner et al., 2005b) suggest that the processing of emotional valence is subserved by the mesolimbic dopaminergic system which can offer at least to some extent a plausible explanation for the poorer performance of CD patients in the valence recognition task.

However, some limitations of the present study have to be addressed. The ratings of sadly and relaxed intonated words ranged low even for HC subjects and thus a potential deficit in processing these emotions in CD could have been missed. Additional studies using complete sentences could help to further elucidate if the described deficit in CD is indeed confined to angrily intonated speech.

In line with the literature (Gundel et al., 2003; Moraru et al., 2002; Jabusch et al., 2004) analysis of the SCL-90-R and BDI scores revealed higher level of psychological distress in dystonic patients with especially pronounced symptoms of somatization, anxiety and depression. Herewith, the question arises if the deficient processing of

angry prosody correlates with the higher level of anxiety and depression. Evidences indicate that increased activity in the orbitofrontal cortex correlates not only with the explicit processing of angrily intonated speech but also with proneness to anxiety reactions (Sander et al. , 2005) Moreover, it is being suggested that patients with social anxiety disorders are less sensitive to facial expression of anger and disgust and that this deficit might even play a role in the development of social anxiety (Montagne et al. , 2006). Therefore, one could speculate that the observed impairment in emotional prosody processing in CD might somehow contribute to the frequently endorsed psychopathological symptoms. On the other hand, anxiety (Lauterbach et al., 2004; Jabusch et al., 2004) and depression (Heiman et al., 2004) may precede or develop independently of the clinical manifestations of dystonia and thus may not be considered as psychoreactive phenomena to a chronic debilitating disease (Gundel et al., 2003; Heiman et al., 2004; Moraru et al., 2002). Jabusch and colleagues (Jabusch et al., 2004) tried to disentangle this last question with regard to anxiety in musicians with focal hand dystonia concluding that anxiety was present before onset of the playing-related disorder. It is further discussed that reduced cortical inhibition might play a role in primary dystonia (Ridding et al. , 1995; Hummel et al. , 2002) as well as in trait anxiety and depression (Wassermann et al. , 2001) implying a possible common pathological background of these conditions. Interestingly, our results did not demonstrate a significant correlation between the performance in the emotional prosody recognition task and CD severity, duration and age of onset or BDI score and SCL-90-R general distress, depression, and anxiety scores implicating that the deficit is rather primary in nature. Likewise, Pedrosa Gil and colleagues (Pedrosa Gil et al. , 2009) noted that neither depression nor anxiety correlated with the accuracy of emotional faces recognition though other studies found inverse correlation of overall

psychological distress and severity of the psychiatric symptoms with the recognition of emotional faces (Csukly et al. , 2008).

Finally, personality evaluation disclosed some specific characteristics of the CD patients. Concerning somatic complaints traits, we replicated the findings of Jabusch and colleagues (Jabusch et al., 2004) with regard to the prominent somatic complaints displayed in CD. In addition, we found accentuated strain and emotionality features in the patient group as well as less pronounced extroversion characteristics. Psychosomatic symptoms reflecting generally more intense perception of bodily sensations seem to be frequently observed in CD patients (Jabusch et al., 2004; Gundel et al., 2003; Moraru et al., 2002). Individuals with higher strain scores are described as feeling overloaded, living in time emergency and constantly confronting with difficult challenges at work and/or personal life. Concerning the emotionality domain dystonia patients appear to be more neurotic, prone to emotional instability and with lowered frustration tolerance. Moreover, CD patients tend to be less extroverted than HC subjects. However, the specific personality traits in CD did not correlate with the severity, duration or age of dystonia onset or with the performance in the emotional prosody recognition task suggesting that individuals with certain personality structure might be rather prone to develop dystonia instead of prominent personality features to evolve as a reaction to a chronic debilitating disease.

In summary the present study demonstrated a deficient processing of emotional prosody recognition in patients with primary cervical dystonia. Furthermore, in line with the literature, dystonia patients displayed more often anxiety, depression and some specific personality features. These findings emphasize the importance to recognize non-motor symptoms in patients with primary focal dystonia and highlight the essential role of basal ganglia in emotional prosody processing.

References

- Alexander GE, Crutcher MD, DeLong MR. Basal ganglia-thalamocortical circuits: parallel substrates for motor, oculomotor, "prefrontal" and "limbic" functions. *Progress in brain research* 1990;85:119-146.
- Breitenstein C, Daum I, Ackermann H. Emotional processing following cortical and subcortical brain damage: contribution of the fronto-striatal circuitry. *Behavioural neurology* 1998;11(1):29-42.
- Bach DR, Grandjean D, Sander D, Herdener M, Strik WK, Seifritz E. The effect of appraisal level on processing of emotional prosody in meaningless speech. *NeuroImage* 2008;42(2):919-927. Breitenstein C, Van Lancker D, Daum I, Waters CH. Impaired perception of vocal emotions in Parkinson's disease: influence of speech time processing and executive functioning. *Brain and cognition* 2001;45(2):277-314.
- Blair RJ, Morris JS, Frith CD, Perrett DI, Dolan RJ. Dissociable neural responses to facial expressions of sadness and anger. *Brain* 1999;122 (Pt 5):883-893.
Baltimore : John Hopkins University, Clinical Psychometrics Research Unit 1977.
- Berardelli A, Rothwell JC, Hallett M, Thompson PD, Manfredi M, Marsden CD. The pathophysiology of primary dystonia. *Brain* 1998;121 (Pt 7):1195-1212.
- Calder AJ, Keane J, Lawrence AD, Manes F. Impaired recognition of anger following damage to the ventral striatum. *Brain* 2004;127(Pt 9):1958-1969.
- Johnson SA, Stout JC, Solomon AC, et al. Beyond disgust: impaired recognition of negative emotions prior to diagnosis in Huntington's disease. *Brain* 2007;130(Pt 7):1732-1744.
- Consky E, Lang A, eds. Clinical assessment in in patients with cervical dystonia. In: Jankovic J, Hallett M, editors. *Therapy with botulinum toxin*. New York: Marcel Dekker, 1994; p. 211-237
- Csukly G, Czobor P, Simon L, Takacs B. Basic emotions and psychological distress: association between recognition of facial expressions and Symptom Checklist-90 subscales. *Comprehensive psychiatry* 2008;49(2):177-183
- Dara C, Monetta L, Pell MD. Vocal emotion processing in Parkinson's disease: reduced sensitivity to negative emotions. *Brain research* 2008;1188:100-111.
- Defazio G, Berardelli A, Hallett M. Do primary adult-onset focal dystonias share aetiological factors? *Brain* 2007;130(Pt 5):1183-1193.
- Derogatis L. SCL-90-R: Administration, scoring and procedures manual-I for the revised version.
- Rinnerthaler M, Benecke C, Bartha L, Entner T, Poewe W, Mueller J. Facial recognition in primary focal dystonia. *Mov Disord* 2006;21(1):78-82.
- Fahn S. Concept and classification of dystonia. *Advances in neurology* 1988;50:1-8.
- Franke G. SCL-90-R – Symptom-Checkliste von L.R. Derogatis – Deutsche Version. Göttingen: Beltz Test. 2., vollständig überarbeitete und neu normierte Auflage 200230.
- Fahrenberg J, Hampel R, Selg H. Das Freiburger Persönlichkeitsinventar FPI, Revidierte Fassung FPI-R und teilweise geänderte Fassung FPI-A1, 7th ed. Göttingen: Hogrefe-Verlag fuer Psychologie; . 2001.
- Gundel H, Wolf A, Xidara V, et al. High psychiatric comorbidity in spasmodic torticollis: a controlled study. *The Journal of nervous and mental disease* 2003;191(7):465-473.

- Goydke KN, Altenmuller E, Moller J, Munte TF. Changes in emotional tone and instrumental timbre are reflected by the mismatch negativity. *Brain research* 2004;21(3):351-359.
- Heiman GA, Ottman R, Saunders-Pullman RJ, Ozelius LJ, Risch NJ, Bressman SB. Increased risk for recurrent major depression in DYT1 dystonia mutation carriers. *Neurology* 2004;63(4):631-637.
- Hummel F, Andres F, Altenmuller E, Dichgans J, Gerloff C. Inhibitory control of acquired motor programmes in the human brain. *Brain* 2002;125(Pt 2):404-420.
- Jabusch HC, Muller SV, Altenmuller E. Anxiety in musicians with focal dystonia and those with chronic pain. *Mov Disord* 2004;19 (10):1169-1175.
- Kotz SA, Meyer M, Alter K, Besson M, von Cramon DY, Friederici AD. On the lateralization of emotional prosody: an event-related functional MR investigation. *Brain and language* 2003;86(3):366-376.
- Lauterbach EC, Freeman A, Vogel RL. Differential DSM-III psychiatric disorder prevalence profiles in dystonia and Parkinson's disease. *The Journal of neuropsychiatry and clinical neurosciences* 2004;16(1):29-36.
- Miller KM, Okun MS, Fernandez HF, Jacobson CE, Rodriguez RL, Bowers D. Depression symptoms in movement disorders: comparing Parkinson's disease, dystonia, and essential tremor. *Mov Disord* 2007;22(5):666-672.
- Montagne B, Schutters S, Westenberg HG, van Honk J, Kessels RP, de Haan EH. Reduced sensitivity in the recognition of anger and disgust in social anxiety disorder. *Cognitive neuropsychiatry* 2006;11(4):389-401.
- Moraru E, Schnider P, Wimmer A, et al. Relation between depression and anxiety in dystonic patients: implications for clinical management. *Depression and anxiety* 2002;16(3):100-103.
- Paulmann S, Pell MD, Kotz SA. Functional contributions of the basal ganglia to emotional prosody: evidence from ERPs. *Brain research* 2008;1217:171-178.
- Pedrosa Gil F, Ridout N, Kessler H, et al. Facial emotion recognition and alexithymia in adults with somatoform disorders. *Depression and anxiety* 2009;26(1):E26-33.
- Pell MD, Leonard CL. Processing emotional tone from speech in Parkinson's disease: a role for the basal ganglia. *Cognitive, affective & behavioral neuroscience* 2003;3(4):275-288.
- Pell MD. Surveying emotional prosody in the brain. In: Bel, B., Marlien, I. (Eds.), *Proceedings of Speech Prosody, 2002 Conference*, 11 -13 April, 2002. Aix-en Provence, Laboratoire Parole et Langage, pp. 77-82. 2002.
- Pell MD, Cheang HS, Leonard CL. The impact of Parkinson's disease on vocal-prosodic communication from the perspective of listeners. *Brain and language* 2006;97(2):123-134.
- Pell MD. On the receptive prosodic loss in Parkinson's disease. *Cortex; a journal devoted to the study of the nervous system and behavior* 1996;32(4):693-704.
- Posner J, Russell JA, Peterson BS. The circumplex model of affect: an integrative approach to affective neuroscience, cognitive development, and psychopathology. *Development and psychopathology* 2005;17(3):715-734.
- Ridding MC, Sheean G, Rothwell JC, Inzelberg R, Kujirai T. Changes in the balance between motor cortical excitation and inhibition in focal, task specific dystonia. *Journal of neurology, neurosurgery, and psychiatry* 1995;59(5):493-498.
- Russell JA. A circumplex model of affect. *Journal of Personality and Social Psychology* 1980;39(11):1161-1178.
- Sander D, Grandjean D, Pourtois G, et al. Emotion and attention interactions in social cognition: brain regions involved in processing anger prosody. *NeuroImage* 2005;28(4):848-858.
- Schroder C, Mobes J, Schutze M, et al. Perception of emotional speech in Parkinson's disease. *Mov Disord* 2006;21(10):1774-1778.

- Speedie LJ, Brake N, Folstein SE, Bowers D, Heilman KM. Comprehension of prosody in Huntington's disease. *Journal of neurology, neurosurgery, and psychiatry* 1990;53(7):607-610.
- Sprengelmeyer R, Rausch M, Eysel UT, Przuntek H. Neural structures associated with recognition of facial expressions of basic emotions. *Proceedings* 1998;265(1409):1927-1931.
- Sprengelmeyer R, Young AW, Calder AJ, et al. Loss of disgust. Perception of faces and emotions in Huntington's disease. *Brain* 1996;119 (Pt 5):1647-1665.
- Wildgruber D, Pihan H, Ackermann H, Erb M, Grodd W. Dynamic brain activation during processing of emotional intonation: influence of acoustic parameters, emotional valence, and sex. *NeuroImage* 2002;15(4):856-869.
- Wassermann EM, Greenberg BD, Nguyen MB, Murphy DL. Motor cortex excitability correlates with an anxiety-related personality trait. *Biological psychiatry* 2001;50(5):377-382.
- Yip JT, Lee TM, Ho SL, Tsang KL, Li LS. Emotion recognition in patients with idiopathic Parkinson's disease. *Mov Disord* 2003;18(10):1115-1122.

Deficient Processing of Emotional Valence in Primary Cervical Dystonia: ERP study

1.1 Abstract

Although primary focal dystonia is perceived by its impact on motor functions, non-motor symptoms affecting cognition and emotionality are recently receiving increased attention. The objective of the present study was to investigate the neurophysiological correlates of emotional prosody recognition in patients with primary cervical dystonia (CD, n=29) in comparison to healthy control subjects (HC, n=29), with regard to processing of valence and arousal affective dimensions. Event-related brain potentials (ERP) were recorded in a modified oddball paradigm under active target detection instructions. As it was predicted the results disclosed a significantly poorer performance of CD patients in classifying emotional prosody. ERP generated by emotional targets (angry, happy, relaxed, and sad) showed significantly smaller P3b amplitudes in CD patients as compared to healthy controls. Moreover, these changes were observed for the recognition of valence but not arousal emotional dimensions of the auditory presented stimuli. These data point to a deficient processing of the valence cues conveying the affective tone in CD and disturbances in the attentive evaluation process across all investigated emotional categories. In line with the literature the findings emphasize the importance of intact basal ganglia function in emotional prosody processing.

1.2 Introduction

Deficits of vocal emotional communication have been frequently reported in movement disorders such as Parkinson's (Ariatti et al., 2008; Dara et al., 2008; Schroder et al., 2006; Yip et al., 2003; Breitenstein et al., 2001,1998; Pell and Leonard, 2003; Pell, 1996; Lloyd, 1999; Blonder et al. , 1989) and Huntington's disease (Sprenghelmeyer et al., 1996; Sprenghelmeyer et al., 1996). These deficits presumably arise from dysfunction of the basal ganglia, which besides its major motor control functions are involved in processing of cognitive and emotional information (Alexander et al., 1990). Indeed, evidence indicates that the striatopallidal structures are integrated into neural circuits subserving processing of emotional prosodic information and are considered to implement a crucial role in affective speech comprehension (Van Lancker Sidtis et al. , 2006; Pell, 2006, Pell, 2002; Pell and Leonard, 2003; Breitenstein et al., 1998). This concept is being consistently supported by numerous studies with Parkinson's disease patients (Dara et al., 2008; Pell and Leonard, 2003; Breitenstein et al., 2001,1998; Pell, 1996), subcortical brain damage patients (Paulmann et al., 2008; Calder et al., 2004; Cancelliere and Kertesz, 1990) and healthy subjects (Bach et al., 2008; Kotz et al., 2003; Wildgruber et al., 2002; Morris et al., 1999). However, while the impairment in emotional prosody processing associated with Parkinson's (PD) and Huntington's (HD) disease has been well studied, findings from other basal ganglia disorders like primary dystonia are still limited. Primary dystonia is a major movement disorder (Fahn, 1988) that is generally considered to exhibit only motor deficits. Its pathophysiology, although not fully understood, has been ascribed mainly to an impaired basal ganglia function and in particular to an overactivity of the direct striatopallidal pathway resulting in reduced globus pallidus internus output (Defazio et al., 2004; Berardelli et al.,

Berardelli et al., 1998). In a previous study (unpublished data) we demonstrated a deficient perception of emotionally spoken words and in particular angrily intoned ones in patients with primary cervical dystonia (CD). Moreover these results were in line with earlier findings of Rinnerthaler et al. (2006) who have reported a deficient recognition of disgust from emotional facial expressions in primary cervical dystonia and blepharospasm patients. It appears that alike other movement disorders the emotional processing in patients with CD is also disturbed. However, the question why only the recognition of particular emotions like anger or disgust seems to be affected in CD remains open. Since the aforementioned studies rely only on analysis of behavioral data some possible response-independent changes of emotional prosody processing might have been missed. In a study investigating emotional prosody perception in Parkinson's disease patients by means of event related brain potentials (ERP), Schroder et al. (2006) have demonstrated significantly lower P3b amplitudes elicited by happily intonated words in the PD group. On the other hand, ERP findings of Paulmann et al. (2008) have not disclosed any significant differences between patients with BG lesions and healthy controls with respect to expectancy positivity potentials (reflecting rapid changes detection of emotional prosodic contours) although the behavioural data have corroborated a deficient emotional prosody processing in the same patient group. So far, the electrophysiological correlates of emotional prosody processing in patients with primary dystonia have not been investigated. If one assumes that CD goes along with deficits in emotional prosody processing, an integrated analysis of behavioral and ERP data could further elucidate if only particular emotions are affected or the deficit is somehow more general in nature. According to the "Circumplex model of affect" (Russell, 1980) all emotions can be interpreted as a linear combination of varying degrees of *valence* (pleasure–displeasure) and *arousal* (high-low) continuum in a two dimensional space. Increasing evidence

supports the existence of distinct neural systems subserving these two dimensions of affect (Gerber et al. , 2008; Posner et al. , 2005). Posner et al. (2005) have suggested two fundamental neurophysiological systems as possible neuroanatomical correlates of the 'circumplex model of affect': the mesolimbic dopaminergic system underlying the processing of emotional valence and the reticular formation (through its connections with the limbic system and thalamus) to be associated with emotional arousal. In a behavioral study of emotional prosody perception in PD, Dara et al., (2008) have demonstrated a poorer performance of PD patients in recognizing the valence of anger, disgust, and fear while the arousal judgements of the same emotions seemed unaffected. The authors argued that a preferential involvement of the basal ganglia in the processing of certain negative emotions irrespective of their degree of arousal may account for the displayed in PD deficient processing of the valence dimension. In line with these findings in a previous study (unpublished data) we observed similar dissociation of impaired emotional prosody comprehension in CD patients associated only with the recognition of valence affective dimension. In contrast, other researchers (Breitenstein et al., 1998) have proposed that prosodic comprehension difficulties in PD might arise from a deficient processing of certain acoustic parameters like increased mean pitch which tends to correlate with arousal comprehension. Hence, the question arises if inefficient processing of certain affective properties of the prosodic information might account for the deficient emotional prosody recognition in CD.

In the present study we aimed to disclose the neurophysiological correlates of emotional prosody processing in CD patients and disentangle the question whether impairment in the affective speech recognition in CD patients is indeed constrained to the deficient processing of only the valence affective dimension. To test the hypothesis that basal ganglia dysfunction would affect the recognition of the valence

features of emotional speech, we conducted an event-related brain potentials study. Due to its excellent time resolution the ERPs technique serves as an ideal tool to investigate the time course of the late “higher” cognitive functions and has already been used to study emotional prosody processing (Kotz and Paulmann, 2007; Schirmer and Kotz, 2006; Schroder et al., 2006; Bostanov and Kotchoubey, 2004; Wambacq and Jerger, 2004).

1.3. Methods

1.3.1 Subjects

Patients with primary cervical dystonia (CD, n=29) and healthy controls subjects (HC, n=29) matched for age, gender and educational level participated in the study. The demographic and clinical data are presented in Table 1. All participants were native German speakers. Dystonia patients were recruited from the botulinum toxin outpatient clinic of the Medical School of Hannover, Germany and classified according to the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) (Consky and Lang, 1994). Only patients with mild to moderate CD (TWSTRS, mean score 24.0 ± 10.5) and minimal or lacking head tremor were investigated. To exclude clinical depression or cognitive impairments all participants underwent Mini Mental State Examination (MMSE) and Beck Depression Inventory (BDI) screening. Subjects scoring lower than 28 on MMSE and higher than 19 on BDI were not recruited. All dystonia patients were receiving botulinum toxin injections every three months. The neurophysiological recordings were performed within two weeks before the next treatment. Additionally, two patients were taking tricyclic antidepressants, one had benzodiazepine, one - anticholinergic medication and one was receiving an antidepressant and benzodiazepine.

All subjects lacked any additional neurological diseases, psychiatric and otolaryngological disturbances.

The study was approved by the local ethics committee and was conducted according to the Declaration of Helsinki. All participants signed a written informed consent.

1.3.2 Stimuli and Experimental design

Different two-syllable words (selected from CELEX database) with semantically neutral content were spoken by two professional actors (male and female) in four different emotional intonations (angry, happy, relaxed, and sad). The auditory material was pre-recorded in a quiet room at 44 kHz AD rate. The acoustic parameters of the stimuli are presented in Table 2. Thirteen frequently used words were chosen in order to avoid similarities in the physical characteristics of the stimuli and to rely on more cognitive judgements of the subjects. The stimuli were validated by 23 naïve listeners who rated separately the *valence* (-2 = very negative, 0 = neutral, +2 = very positive) and *arousal* (-2 very calm, 0= neutral, +2 = very excited) dimensions as well as the emotional category (angry, happy, relaxed, sad) of the affective intonation. Only consistent evaluations were used for the experiment. The emotionally intonated words were arranged pseudo-randomly in a modified oddball (context violation) paradigm with a probability of 0.8 for the frequent standard (std) and of 0.2 for the rare deviant (dev) stimuli. A total of 800 words were presented in four blocks. Each block comprised 200 words (std/dev, 160/40) as each emotion was introduced as standard and deviant stimulus and presented 200 times as a total. The std-dev stimuli in each block differed by their opposite valence (positive-negative) in valence condition and

Table 1: Demographic and clinical data

	Controls	Dystonia
	29	29
Age, yr	55.9 (8.3)	56.2 (8.8)
Gender f/m	16/12	16//12
Education, yr	12.6 (2.5)	10.6 (1.7)
MMSE	29.6 (0.5)	29.1 (0.8)
BDI	4.7 (5.3)	8.6 (4.7)
TWSTRS	na	24.0 (10.5)
Duration, yr	na	10.7 (9.0)
Age of onset, yr	na	45.8 (11.7)

Data presented as mean values (SD). CD, Cervical dystonia; HC, healthy controls; MMSE, Mini-Mental State Examination; BDI, Beck Depression Inventory; TWSTRS, Toronto Western Spasmodic Torticollis Rating Scale.

opposite arousal (calm-exited) in arousal condition respectively (see Table 3). The emotionally intonated words were delivered with an ISI of 2500 ms considered from stimulus onset. In order to avoid higher error rates for a particular emotion due to fatigue at the end of the experimental session, blocks were presented in an alternating succession. The study involved two experimental conditions. In the valence condition the participants were asked to rate the emotional prosody of each presented word, as positive or negative and in the arousal condition as exited or calm respectively, by pressing one of three keyboard buttons with a third possible response “I do not know”. Each subject participated in one of the two experimental conditions as the subgroups were matched for age, gender and educational level. There was no

significant difference for BDI and MMSE scores, as well as for CD duration, age of onset and TWSTRS score between the two subgroups.

Response latencies were measured from sound onset with the time-out point (time after which responses were registered as missing) set at 2500 ms.

Table 2: Acoustic parameters of the stimuli

Stimuli	Intensity (dB)	Pitch (Hz)	Duration (ms)
Angry	76.7 (2.5)	203.0 (49.2)	642.4 (122.7)
Happy	77.2 (3.4)	216.4 (57.5)	695.6 (341.6)
Relaxed	76.7 (3.2)	157.1 (42.5)	1053.6 (341.6)
Sad	76.0 (3.2)	178.6 (57.7)	664.6 (195.9)

Table 3: Experimental paradigm

	Valence		Arousal	
	standards	deviants	standards	deviants
Block I	angry	happy	angry	sad
Block II	happy	angry	happy	relaxed
Block III	relaxed	sad	relaxed	happy
Block IV	sad	relaxed	sad	angry

1.3.3 ERP acquisition and analysis

The brain electrical activity was recorded by means of 'Neuroscan' system (Herndon, Virginia, USA) with 250Hz A/D conversion rate and analogue filter pass band 0.05 - 50Hz. The EEG acquisition was carried out using 'Easy cap' (EASYCAP GmbH, Herrsching-Breitbrunn, Germany) and 31Ag/AgCl electrodes placed on the scalp according to the extended international 10-20 system (Jasper, 1958). The impedance was measured for all electrodes before the EEG acquisition and kept under 5kOhm during the entire recording procedure. The common reference electrode was positioned at the left mastoid process and two additional electrodes were placed infraorbitally and at the lateral canthus of the left eye for monitoring of the electro-ocular activity. Data were analysed and averaged off-line using EEGLAB software (Delorme and Makeig, 2004) after digital filtering with 0.1 - 30 Hz and artefacts rejection was carried out. EEG epochs were time-locked to the stimulus onset for a time window of 1500 ms including 500 ms pre-stimulus interval and the baseline was corrected for the -500 ms pre-stimulus period. Electroocular artefacts (ocular movements and eye blinks) and signal contaminating muscle activity were corrected using blind source separation algorithm implicating canonical correlation analysis (Gómez-Herrero et al. , 2006; De Clercq et al. , 2006). As the research hypotheses focuses on the P300 (P3b) component, we do not describe the elicited P200 and N400 waveforms. Further on in that paper we refer to the P3b component, defined as the largest positive-going peak occurring within 250-500 ms latency range with a peak amplitude maximum at parietal electrode sites.

1.4 Results

The P3b component mean amplitudes, quantified for a time window of 250-440ms at Fz, Cz and Pz electrode sites, were implemented for statistical evaluation. Repeated measures analysis of variance (ANOVA) was performed including the factors *emotion* (angry, happy, relaxed, sad) and *electrode site* (Fz, Cz, Pz) as within-subject factors and *group* (HC, CD) as between-subject factor. Huynh-Feldt epsilon correction was used when appropriate. P values smaller than 0.05 were considered significant.

1.4.1 Valence condition - P3b component

Significant group differences with a main effect for factor *Group* were obtained for both standards ($F(1,120) = 18.687, p = 0.000$) and deviants ($F(1,120) = 16.457, p = 0.000$). The factor *Electrode* also yielded a significant main effect for both the frequent ($F(1,592) = 9.159, p = 0.001$) and the rare ($F(1,533) = 11.879, p = 0.000$) stimuli. Additionally, a significant interaction between the factors *Group* and *Electrode* was observed for the standard ($F(1,592) = 9.403, p = 0.000$) as well as for the deviant stimuli ($F(1,533) = 4.833, p = 0.016$). No significant Group x Emotion x Electrode interaction effect was not observed neither for the standards nor for the deviants. Furthermore, to compare group differences for each emotion two tailed t-test for independent samples was applied for the central and posterior meadline electrodes. Analysis revealed significantly lower mean amplitudes in CD group at Pz electrode site for all four emotions besides for angry deviants stimuli: angry std (CD, $M = -0.84$; HC, $M = 3.38$; $p = 0.01$), happy std (CD, $M = -0.31$; HC, $M = 3.10$; $p = 0.011$), relaxed std (CD, $M = -1.21$; HC, $M = 1.88$; $p = 0.05$), sad std (CD, $M = -1.44$; HC, $M = 2.12$; $p =$

0.001), happy dev (CD, $M = -0.98$; HC, $M = 2.95$; $p = 0.000$), relaxed dev (CD, $M = -1.73$; HC, $M = 1.98$; $p = 0.001$), sad dev (CD, $M = -1.54$; HC, $M = .85$; $p = 0.036$). Additionally the same effect was observed at Cz electrode for angry std (CD, $M = -1.55$; HC, $M = 2.03$; $p = 0.031$) and sad std (CD, $M = -1.75$; HC, $M = 1.40$; $p = 0.025$) as well as trend values for happy std, $p = 0.082$ and relaxed std, $p = 0.064$ stimuli. The deviant stimuli demonstrated significant effect at the Cz electrode only for happy (CD, $M = -1.39$; HC, $M = 2.22$; $p = 0.008$) and relaxed (CD, $M = -1.75$; HC, $M = 1.27$; $p = 0.027$) emotions respectively. Results are presented on Fig. 1A and 2A. The data indicate that in valence condition, the significant group differences involve mainly the posterior electrode sites but also spread to the central electrode sites and is more pronounced for the standard stimuli.

1.4.3 Arousal condition - P3b component

Arousal condition (Fig.1B and 2B) yielded significant differences with main effect of the *Group* factor ($F(1,96) = 6.980$, $p = 0.010$) for the standard but not for the deviant tones. Likewise, in the valence condition factor *Electrode* reached significant levels for both the standards ($F(1,865) = 18.959$, $p = 0.000$) and the deviants ($F(1,678) = 10,787$, $p = 0.000$). Significant effect of *Electrode* \times *Group* interaction was observed again for both the frequent ($F(1,865) = 3.993$, $p = 0.23$) and the rare ($F(1,678) = 4.886$, $p = 0.13$) prosodic stimuli. No significant *Group* \times *Emotion* \times *Electrode* interaction effect was found for both standards and deviants. The main Group effect of the standard tones was further evaluated by independent samples t- test (two tailed) for the central and posterior electrodes but results did not reach significant values.

Additionally, paired t-test (two tailed) was performed to compare the P3b amplitudes at the left and right hemisphere' frontal, central and posterior electrode

sites (F3-F4, C3-C4, P3-P4). Results did not show significant differences for both groups and both tasks (valence and arousal), indicating a lack of lateralization effect for any of the four emotions.

1.4.3 Behavioral data

Proportions of correct responses were obtained and compared by t-Test for independent samples (two tailed). Additionally, linear Pearson's rho analysis was employed to correlate the performance in CD for both experimental conditions with the BDI and the TWSTRS scores as well as with the age of onset and duration of the dystonia.

The results for the valence condition disclosed significantly poorer performance of the dystonia patients on the emotional prosody recognition task for angry standard (CD, $M = 0.42$; HC, $M = 0.63$; $p = 0.030$) and angry deviant (CD, $M = 0.45$; HC, $M = 0.76$; $p = 0.003$) prosodic stimuli. No significant differences were found for the other emotions. Arousal condition did not demonstrate any significant between group differences.

Finally, no significant correlations were found between BDI score and the performance of emotional prosody recognition in CD patients. Moreover, the ratings of the affective tone across all emotions for both conditions did not correlate with the disease severity, duration and age of onset of the dystonia.

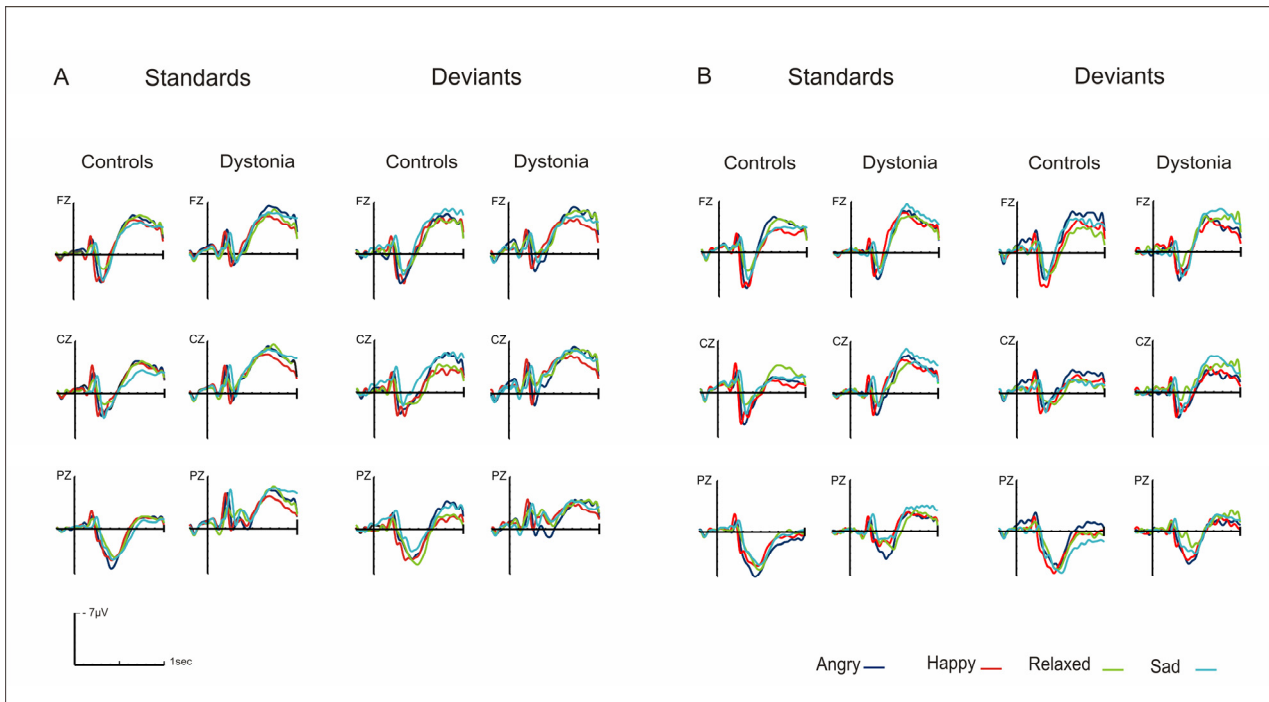


Fig.1 Grand average waveforms of healthy controls for A) *Valence* and B) *Arousal* condition. The event related brain potentials are shown for both standard and deviant stimuli at Fz, Cz, and Pz electrode sites across all emotional categories. Note the large P3b component at 250-500ms latency range with a pick amplitude maximum at Pz site.

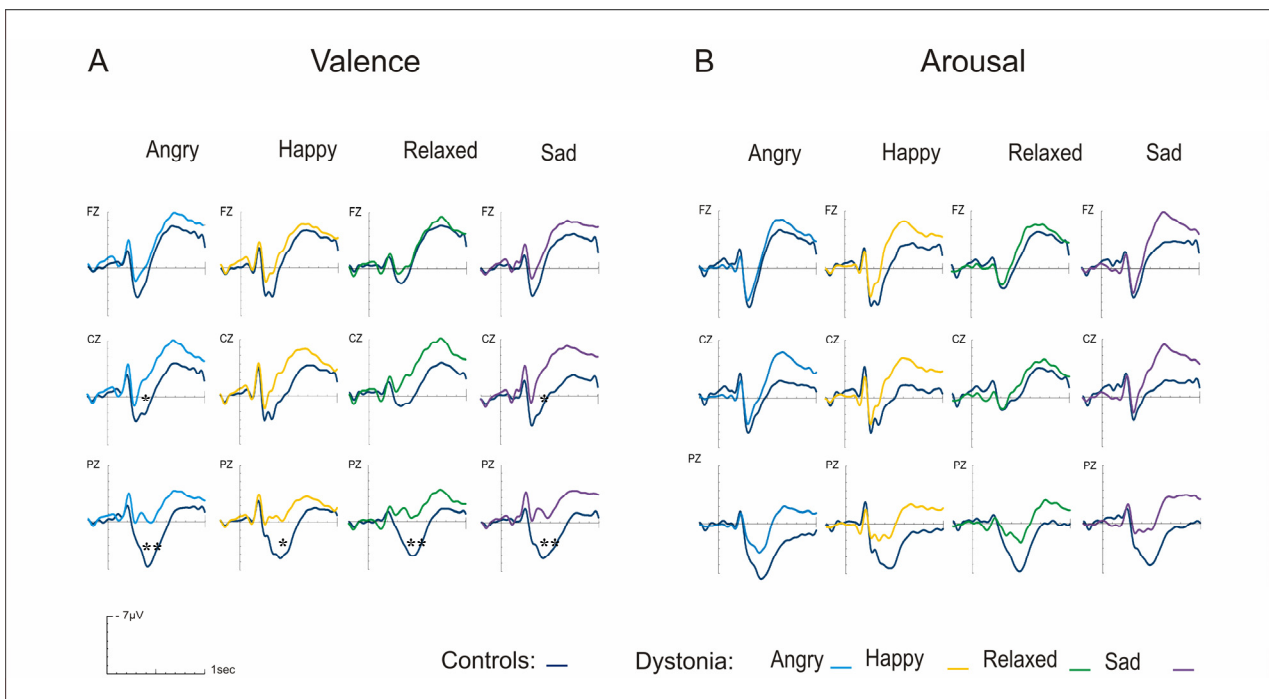


Fig. 2 Grand average waveforms of cervical dystonia patients (CD) and healthy controls (HC) shown for the standard stimuli at three midline electrode sites. Note the significant difference between CD and HC of the P3b component at Pz and Cz electrode sites for the (A) *valence* but not the (B) *arousal* condition (* $p < 0.05$, ** $p < 0.01$).

1.5 Discussion

The present study revealed an impairment of emotional prosody processing in patients with primary cervical dystonia who demonstrated significantly poorer performance in classifying emotionally intonated words as compared to HC subjects. Importantly, as indicated by both behavioural and neurophysiologic data, this deficit was found only for the valence judgements of emotional tone whereas in the arousal task no group differences were observed. Moreover, while in the valence condition the behavioural data disclose deficient processing of angry prosody the obtained ERPs revealed significantly diminished P3b amplitudes in the CD group across all investigated emotional categories (angry, happy, relaxed and sad).

The P3b component is normally associated with target evaluation and categorization processes (Luck, 2005). It is also considered to be a sensitive measure of subject's capacity to allocate attentional resources towards a certain stimulus (Johnson et al., 2004). Accordingly, the more efforts the subject devotes to a difficult task the larger the P3b component. However its amplitude may attenuate if the subject is less certain about the category of a given stimulus and dedicates more efforts for its evaluation (Luck, 2005). Therefore it might be assumed that the deficit in emotional prosody recognition as reflected by smaller P3b mean amplitudes in CD might partly be related to somewhat limited abilities of CD patients to allocate their attentional resources under higher demand processing task. In this respect, Scott et al. (2003) have reported the presence of selective attentional – executive deficit in patients with primary dystonia, who have displayed significant attentional set-shifting impairment. Likewise, Duane and Vermilion (2004) in a study investigating the affect and cognition in CD patients with tremor, have described a prominent deficit with regard to the visual attention in that particular group.

According to [Schirmer and Kotz \(2006\)](#) vocal emotional processing comprises basic analysis of acoustic information like frequency, intensity and temporal information that occur within the first 100 ms after stimulus onset, followed by integration of those acoustic cues and encoding of their emotional significance occurring at approximately 200 ms. The derived emotional significance is then available for higher order cognitive processes, such as evaluative judgments mediated by the right inferior and orbitofrontal cortex or semantical processing. Hence, the observed changes of the P3b component in CD patients point to a deficit at the late, “higher” attention-dependent cognitive stages in the emotional prosody processing. Importantly, as it was predicted, the emotional processing deficit appeared to be task specific. Namely, the P3b amplitude was significantly smaller only when CD patients rated the valence dimension of the emotional tone while there was not difference between the two groups for the arousal task across any of the four emotions. Moreover, these results are in agreement with our previous findings (unpublished data) demonstrating poorer performance of CD patients only for the valence but not the arousal classification task. Hence the data of the present study disclose altered emotional prosody recognition in CD that appears to be rather specific and constrained to the perception of valence affective dimension. The question arises how this specific deficit in processing the valence cues of the emotional prosodic contour might be explained in a disorder involving basal ganglia dysfunction. In a behavioral study on emotional prosody perception [Dara et al. \(2008\)](#) have reported a similar dissociation of these two affective dimensions in PD patients. The authors demonstrated a poorer performance of PD patients in recognizing anger, disgust, and fear by assigning significantly higher valence ratings to these emotions than the healthy control group while there were not differences in rating the communicated arousal emotional features. Moreover it is being further suggested that a preferential

involvement of the basal ganglia in processing certain negative emotions, irrespective of their intensity of expression might account for the misjudgement of only valence affective dimension in PD. In line with these findings in the present study the behavioral data indeed showed only a deficient evaluation of the valence of angrily intonated words. However, ERP analysis points to a more general deficit as the mean amplitudes of the P3b component elicited in the valence task were diminished for all investigated emotional categories including those with positive valence (happy and relaxed). One possible explanation for the specific impairment in CD for the recognition of only the valence dimension might be derived from the concept of [Posner et al. \(2005\)](#) suggesting two fundamental neurophysiological systems that might serve as neuroanatomical correlates of the 'circumplex model of affect': the mesolimbic dopaminergic system underlying the processing of emotional valence and the reticular formation (through its connections with the limbic system and thalamus) to be associated with emotional arousal. The dopaminergic neurons of the mesolimbic system originating from the ventral tegmental area spread their projections to nucleus accumbens, regarded as the main constituent of the ventral striatum (also referred to as extended limbic system) which in turn is integrated in the cortico-striatal-thalamo-cortical limbic loop considered to play a role in emotional processing ([Alexander et al., 1990](#)). Moreover, even though the pathophysiology of primary dystonia is complex and yet not fully understood, it is attributed mainly to basal ganglia dysfunction and more specifically to overactivity of the direct striatopallidal pathway resulting in reduced globus pallidus internus output and abnormal cortical excitability ([Defazio et al., 2007](#); [Berardelli et al., 1998](#)). Therefore the mesolimbic projections to the ventral striatum might also be somehow engaged in these dysfunctional processes, resulting in a deficient processing of the valence features of emotional prosody. Future studies using functional neuroimaging techniques might help to bring further insight on the

neuroanatomical systems subserving the valence and arousal processing.

Besides the idea of valence and arousal specific neuronal networks an alternative explanation for the deficient emotional prosody recognition in CD might be that dystonic patients are not able to process as efficiently the physical acoustic patterns that constitute the prosodic valence of an emotional stimulus. The decoding of emotional prosody is a complex process that requires analysis and integration of a variety of acoustic cues, among which intensity, duration and fundamental frequency (Fo) seem to play the most important role (Banse and Scherer, 1996; Scherer, 1986). It is being well established that a high level of physiological arousal is associated with high mean fundamental frequency (Fo), higher Fo variability and increased vocal intensity (Bachorowski, 1999; Scherer et al. , 1991). However, emotions associated with high arousal but different valence can be distinguished by different patterns of Fo changes over the time course of an emotional utterance with a decreasing Fo for negative and increasing Fo for positive emotions. Hence the demonstrated deficits in CD patients in the valence task might arise from inefficient processing of the temporal cues conveying the presented speech signal. Support for this idea might be drawn from previous research in patients with Parkinson's disease (Breitenstein et al. 2001) which have demonstrated impairment in processing of speech rate information implying an increased temporal discrimination threshold and underestimation of time interval durations in PD patients. Recent findings in primary dystonia elicited ERPs in have disclosed the presence of temporal discrimination disturbances with increased temporal discrimination threshold to somatosensory stimulation (Defazio et al., 2007, Tinazzi et al., 2002). Therefore, it is possible that the deficient emotional prosody recognition in CD arises from inefficient temporal discrimination of one/more acoustic parameters like detection of rapid pitch changes in emotional prosodic contours or evaluation of temporal cues that are important for valence discrimination. Future

studies using stimuli with systematic modulation of temporal and spectral cues of emotional prosody could help to further elucidate if this phenomenon indeed holds true for patients with primary focal dystonia.

Finally, the question of concomitant mood disorders, as one possible and often discussed confound when investigating emotional processing in patients with movement disorders has to be considered. Taking into account that subjects suffering from depression were excluded from the experiment as well as the lack of correlation between the emotion recognition tasks and the BDI scores, it seems that the displayed in CD deficits in emotional prosody recognition does not arise from a depressive state. Moreover, the performance of CD patients on the arousal recognition task did not differ significantly from the healthy control group. Likewise, dystonia severity, duration and age of onset did not correlate with the behavioural data for both experimental conditions suggesting that the emotion recognition impairment does not appear to be a secondary, reactive phenomenon to a chronic and debilitating disease but rather primary in nature.

In conclusion, consistent with previous research on emotional prosody processing in other basal ganglia disorders, the present study disclosed a deficit in emotional prosody recognition in patients with primary cervical dystonia. As indicated by the elicited ERPs in the patient group it appears that the impairment engages the late attentive processing stages and might arise from a limited reallocation of attentional resources in CD under the high demanding task of emotional prosody processing. Importantly, the described deficit seems to be restricted to the recognition of the valence dimension of affective prosody sparing the ability to identify the degree of arousal conveying the emotional tone. It is noteworthy that in the valence task the disclosed by the elicited ERPs deficit in CD involved all investigated emotions (happy, angry, relaxed, sad) suggesting that the disturbed emotional prosody comprehension

in CD patients is rather general in nature than restricted to the processing of distinct emotional categories like results of former studies imply. Taken together these findings provide further insights in the important contribution of the basal ganglia circuits in emotional prosody processing.

References

- Alexander GE, Crutcher MD, DeLong MR. Basal ganglia-thalamocortical circuits: parallel substrates for motor, oculomotor, "prefrontal" and "limbic" functions. *Progress in brain research* 1990;85:119-146.
- Ariatti A, Benuzzi F, Nichelli P. Recognition of emotions from visual and prosodic cues in Parkinson's disease. *Neurol Sci* 2008;29:219-227.
- Bach DR, Grandjean D, Sander D, Herdener M, Strik WK, Seifritz E. The effect of appraisal level on processing of emotional prosody in meaningless speech. *NeuroImage* 2008;42:919-927.
- Bachorowski JA. Vocal expression and perception of emotion. *Current Direct. Psychol. Sci.* 8 (2), 53–57. 1999.
- Banse R, Scherer KR. Acoustic profiles in vocal emotion expression. *Journal of personality and social psychology* 1996;70:614-636.
- Berardelli A, Rothwell JC, Hallett M, Thompson PD, Manfredi M, Marsden CD. The pathophysiology of primary dystonia. *Brain* 1998;121 (Pt 7):1195-1212.
- Blonder LX, Gur RE, Gur RC. The effects of right and left hemiparkinsonism on prosody. *Brain and language* 1989;36:193-207.
- Bostanov V, Kotchoubey B. Recognition of affective prosody: continuous wavelet measures of event-related brain potentials to emotional exclamations. *Psychophysiology* 2004;41:259-268.
- Breitenstein C, Daum I, Ackermann H. Emotional processing following cortical and subcortical brain damage: contribution of the fronto-striatal circuitry. *Behavioural neurology* 1998;11:29-42.
- Breitenstein C, Van Lancker D, Daum I, Waters CH. Impaired perception of vocal emotions in Parkinson's disease: influence of speech time processing and executive functioning. *Brain and cognition* 2001;45:277-314.
- Calder AJ, Keane J, Lawrence AD, Manes F. Impaired recognition of anger following damage to the ventral striatum. *Brain* 2004;127:1958-1969.
- Cancelliere AE, Kertesz A. Lesion localization in acquired deficits of emotional expression and comprehension. *Brain and cognition* 1990;13:133-147.
- Consky E, Lang A. Clinical assessments of patients with cervical dystonia. In: Jankovic J, Hallett M, Editors *Therapy with botulinum toxin*. New York: Marcel Dekker; 1994;211–237
- Dara C, Monetta L, Pell MD. Vocal emotion processing in Parkinson's disease: reduced sensitivity to negative emotions. *Brain Res* 2008;1188:100-111.
- De Clercq W, Vergult A, Vanrumste B, Van Paesschen W, Van Huffel S. Canonical correlation analysis applied to remove muscle artifacts from the electroencephalogram. *IEEE transactions on bio-medical engineering* 2006;53:2583-2587.
- Defazio G, Abbruzzese G, Livrea P, Berardelli A. Epidemiology of primary dystonia. *Lancet neurology* 2004;3:673-678.
- Defazio G, Berardelli A, Hallett M. Do primary adult-onset focal dystonias share aetiological factors? *Brain* 2007;130:1183-1193.

- Delorme A, Makeig S. EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of neuroscience methods* 2004;134:9-21.
- Duane DD, Vermilion KJ. Cognition and affect in patients with cervical dystonia with and without tremor. *Advances in neurology* 2004;94:179-189.
- Fahn S. Concept and classification of dystonia. *Advances in neurology* 1988;50:1-8.
- Gómez-Herrero G, Clercq WD, Anwar H, Kara O, Egiazarian K, Huffel SV, Paesschen WV. Automatic removal of ocular artifacts in the eeg without a reference eeg channel. In *Proc. NORSIG2006, Reykjavik, Iceland*; p. 130–133.
- Gerber AJ, Posner J, Gorman D, Colibazzi T, Yu S, Wang Z, Kangarlu A, Zhu H, Russell J, Peterson BS. An affective circumplex model of neural systems subserving valence, arousal, and cognitive overlay during the appraisal of emotional faces. *Neuropsychologia* 2008;46:2129-2139.
- Kotz SA, Meyer M, Alter K, Besson M, von Cramon DY, Friederici AD. On the lateralization of emotional prosody: an event-related functional MR investigation. *Brain and language* 2003;86:366-376.
- Kotz SA, Paulmann S. When emotional prosody and semantics dance cheek to cheek: ERP evidence. *Brain Res* 2007;1151:107-118.
- Lloyd AJ. Comprehension of prosody in Parkinson's disease. *Cortex; a journal devoted to the study of the nervous system and behavior* 1999;35:389-402.
- Luck SJ. *An introduction to the event-related potential technique* 2005. Cambridge, MA: MIT; p. 43-44.
- Morris JS, Scott SK, Dolan RJ. Saying it with feeling: neural responses to emotional vocalizations. *Neuropsychologia* 1999;37:1155-1163.
- Paulmann S, Pell MD, Kotz SA. Functional contributions of the basal ganglia to emotional prosody: evidence from ERPs. *Brain research* 2008;1217:171-178.
- Pell MD. Cerebral mechanisms for understanding emotional prosody in speech. *Brain and language* 2006;96:221-234.
- Pell MD. On the receptive prosodic loss in Parkinson's disease. *Cortex; a journal devoted to the study of the nervous system and behavior* 1996;32:693-704.
- Pell MD. Surveying emotional prosody in the brain. In: Bel, B., Marlien, I. (Eds.), *Proceedings of Speech Prosody, 2002 Conference*, 11 -13 April, 2002. Aix-en Provence, Laboratoire Parole et Langage, pp. 77-82. 2002.
- Pell MD, Leonard CL. Processing emotional tone from speech in Parkinson's disease: a role for the basal ganglia. *Cognitive, affective & behavioral neuroscience* 2003;3:275-288.
- Posner J, Russell J, Peterson B. The circumplex model of affect: an integrative approach to affective neuroscience, cognitive development, and psychopathology. *Development and psychopathology* 2005;17:715-734.
- Rinnerthaler M, Benecke C, Bartha L, Entner T, Poewe W, Mueller J. Facial recognition in primary focal dystonia. *Mov Disord* 2006;21:78-82.
- Russell JA. A circumplex model of affect. *Journal of Personality and Social Psychology* 1980;39
- Scherer KR. Vocal affect expression: a review and a model for future research. *Psychological bulletin* 1986;99:143-165.
- Scherer KR, Banse R, . HGW, Goldbeck T. Vocal cues in emotion encoding and decoding. *Motiv. Emot.* 1991; 15 (2), 123–148. Schirmer A, Kotz SA. Beyond the right hemisphere: brain mechanisms mediating vocal emotional processing. *Trends in cognitive sciences* 2006;10:24-30.
- Schroder C, Mobes J, Schutze M, Szymanowski F, Nager W, Bangert M, Munte TF, Dengler R. Perception of emotional speech in Parkinson's disease. *Mov Disord* 2006;21:1774-1778.

- Scott RB, Gregory R, Wilson J, Banks S, Turner A, Parkin S, Giladi N, Joint C, Aziz T. Executive cognitive deficits in primary dystonia. *Mov Disord* 2003;18:539-550.
- Sprengelmeyer R, Young AW, Calder AJ, Karnat A, Lange H, Homberg V, Perrett DI, Rowland D. Loss of disgust. Perception of faces and emotions in Huntington's disease. *Brain* 1996;119 (Pt 5):1647-1665.
- Tinazzi M, Rosso T, Fiaschi A, Gambina G, Farina S, Fiorio SM, Aglioti SM. The role of somatosensory feedback in dystonia: a psychophysical evaluation. *Neurol Sci* 2002;23 Suppl 2:S113-114.
- Van Lancker Sidtis D, Pachana N, Cummings JL, Sidtis JJ. Dysprosodic speech following basal ganglia insult: toward a conceptual framework for the study of the cerebral representation of prosody. *Brain and language* 2006;97:135-153.
- Wambacq IJ, Jerger JF. Processing of affective prosody and lexical-semantics in spoken utterances as differentiated by event-related potentials. *Brain research* 2004;20:427-437.
- Wildgruber D, Pihan H, Ackermann H, Erb M, Grodd W. Dynamic brain activation during processing of emotional intonation: influence of acoustic parameters, emotional valence, and sex. *NeuroImage* 2002;15:856-869.
- Yip JT, Lee TM, Ho SL, Tsang KL, Li LS. Emotion recognition in patients with idiopathic Parkinson's disease. *Mov Disord* 2003;18:1115-1122.

Discussion

To our knowledge, the present study is the first one addressing the emotional information processing via the auditory communication channel in patients with primary cervical dystonia. By employing behavioral and neurophysiological methods, we aimed to find out if CD patients, similarly to other movement disorders, encounter difficulties in recognizing the emotional tone from vocal expressions. In addition, we sought to determine possible correlations between the performance of CD patients in the affective prosody recognition task with their psychological status and personality profile. Analysis of behavioral data disclosed a significantly poorer performance of emotional prosody recognition in CD and particularly in rating angrily intonated words. Moreover, the judgments of angry emotional tone in the CD group were accompanied by significantly slower reaction times. Hence, these findings point to a deficient perception of angry intonation in patients with primary cervical dystonia. In addition, event-related brain potentials were recorded under active target detection instructions. The elicited ERPs have further corroborated the deficient emotional prosody processing in CD. Moreover, the generated in CD P3b component showed significantly reduced amplitudes across all investigated emotions suggesting that the impaired emotional prosody recognition is not constrained to a specific emotional category but is rather more generally affected. Interestingly, the deficient emotional

prosody processing was observed only when judging the valence but not the arousal emotional dimension. It is noteworthy that this dissociation was demonstrated by both the behavioral and the neurophysiological findings. Taking into account the aforementioned results, there are several questions that need to be addressed. First, how changes of emotional prosody processing can be explained in a disorder which is considered predominantly motor; second, is emotional processing in CD more generally affected or the observed deficit is rather constrained to specific emotional categories; and third, why patients with primary cervical dystonia display deficits in rating valence but not the arousal features conveying a vocal emotional message.

A large body of evidence indicates that the basal ganglia play a crucial role in emotional prosody processing. This notion has gained support from number of studies with Parkinson's disease patients (Ariatti et al., 2008; Dara et al., 2008; Schroder et al., 2006; Yip et al., 2003; Breitenstein et al., 2001, 1998; Pell, 1996, 2002, 2003; Lloyd, 1999; Blonder et al., 1989), Huntington's disease (Sprengelmeyer et al., 1996; Speedie et al., 1990) and patients with subcortical brain lesions (Cancelliere and Kertesz, 1990; Paulmann et al., 2008; Calder et al., 2004). Likewise, recent neuroimaging studies has revealed bilateral involvement of putamen and caudate nucleus (Kotz et al., 2003) as well as pallidum and anterior insula (Wildgruber et al., 2002) in the perception of emotional prosody. Moreover, it has been suggested that different appraisal levels of emotional prosody processing are subserved by amygdala-prefrontal-cingulate network and that the anterior cingulate cortex (Bach et al., 2008) and the basal ganglia implement a specific role in the explicit emotional prosody identification (Bach et al., 2008; Paulmann et al., 2008). Further support for the concept that fronto-striatal circuits are particularly involved in emotional processing (Alexander et al., 1990; Lalande et al., 1992; Weddell, 1994) have been

provided by Breitenstein et al. (1998) in a study with PD patients and patients with subcortical brain damage. The authors concluded that contributions of the prefrontal and limbic cortico-striatal-thalamo-cortical connections and particularly the lateral orbitofrontal loop implicated in cognitive and emotional processes (Crosson, 1992) might be responsible for the deficient emotional processing in patients with PD. Given the putative involvement of the striatopallidal structures in processing of emotional prosodic information and the pathophysiologic correlates of primary focal dystonia associated mainly with basal ganglia dysfunction it is not surprising that patients with primary cervical dystonia display deficit in the emotional prosody comprehension. Therefore, our results are consistent with the hypothesis that CD patients would encounter difficulties in decoding the emotional intonation, hence, providing further evidence for basal ganglia involvement in emotional prosody processing.

Given the findings of the present study, another question to be addressed is why the displayed deficit was associated with the valence but not the arousal affective dimension. Indeed, as it was hypothesized, our results revealed rather specific impairment of emotional processing that appeared to be constrained only to the valence dimension. Moreover, this phenomenon was observed in both behavioral and neurophysiologic experiments. Interestingly, in a behavioral study on emotional prosody perception with PD patients, Dara et al. (2008) have reported a similar dissociation of these two affective dimensions. The authors have demonstrated a poorer performance of PD patients in the recognition of anger, disgust and fear when judging the valence but not the arousal features of these emotions, suggesting a preferential involvement of the basal ganglia in processing certain negative emotions, irrespective of their intensity. However, in contrast to the latter findings the present results demonstrated a deficit across all emotional categories including those with

positive valence (happy and relaxed). One possible explanation for an impairment in judging only the valence acoustic features might be given by the concept of [Posner et al. \(2005\)](#) suggesting two fundamental neurophysiological systems serving as a neuroanatomical correlates of the 'circumplex model of affect': the mesolimbic dopaminergic system underlying the processing of emotional valence and the reticular formation (through its connections with the limbic system and thalamus) to be associated with emotional arousal. The mesolimbic system originates from the ventral tegmental area and spreads its dopaminergic projections to nucleus accumbens, considered a main constitute of the ventral striatum (also referred to as extended limbic system). The ventral striatum itself is integrated into the cortico-striatal-thalamo-cortical limbic loop considered to play a role in emotional processing ([Alexander et al., 1990](#)). Taking into account that the pathophysiology of primary dystonia is ascribed mainly to basal ganglia dysfunction ([Berardelli et al., 1998](#); [Defazio et al., 2007](#)), it seems reasonable to assume that a possible involvement of the mesolimbic projections in that process may at least to some extent account for the specific deficit in CD associated with the recognition of the valence affective dimension.

Another question that arises when taking into consideration the results of the present study is whether the dystonic patients' impairment to appropriately interpret prosodic aspects of speech is rather selective or somehow more general in nature. Considering the behavioural data, the results disclosed deficient recognition of vocal expressions in CD which appeared to be constrained to angry prosody therefore supporting somewhat the concept of separable emotion specific neuronal networks subserving the processing of distinct basic emotions ([Sprengelmeyer et al., 1998](#); [Blair et al., 1999](#)). On the other hand the neurophysiological findings indicated more

general impairment in affective functioning and the processing of various types of emotional categories. According to [Scherer et al., \(1991\)](#) ratings of vocal emotional expressions obtained from actor portrayals by naïve listeners demonstrate that a reliable acoustic differentiation of the major basic emotions is possible. It has been further suggested that the most salient attribute to allow for prosody classification is the arousal factor, realized by a higher mean fundamental frequency (Fo), Fo range and high-frequency spectral energy of the speech signal. In line with Scherer's disclosures, the behavioral data in the present study revealed that both groups' ratings of low arousal prosodic stimuli (sad, relaxed) were less accurate than those of high arousal (angry, happy). However, since relaxed and sadly intonated words were often misjudged even from the HC subjects a potential difference in processing of sad and relaxed prosody in primary dystonia could have been missed. Indeed, the neurophysiologic data disclosed somehow broad-based deficit in the ability of dystonic patients to process emotions from vocal cues. It is possible that the ERPs detect more subtle and concealed changes in emotional processing related to higher cognitive demands of subjective rating tasks than the behavioural responses could display.

Finally, another aspect of the present research was to consider the psychological status and personality profile of CD patients and to determine possible correlations with the performance of emotional prosody recognition. A number of complementary studies suggest that primary dystonia is associated with a higher prevalence of psychiatric disorders, particularly anxiety and depression ([Miller et al., 2007](#); [Lauterbach et al., 2004](#); [Gundel et al., 2003](#); [Jabusch et al., 2004](#); [Moraru et al., 2002](#)). However, so far no conclusive data exist to answer the question if depression, anxiety or specific personality traits correlate with deficits in emotional processing. We tried to unravel this matter by employing neurophysiological testing of CD patients and

than correlating the scores with the behavioural responses. Interestingly, our results did not demonstrate a significant correlation between the performance on emotional prosody recognition task and neither the BDI, SCL-90-R general distress index, depression and anxiety scores nor CD severity, duration and age of onset, indicating that the emotional processing deficit is rather primary in nature and not a consequence of the chronic disease. Moreover, the performance of CD patients did not differ significantly from the healthy control group on the arousal recognition task. Likewise, other authors have also noted that neither depression nor anxiety had correlated with the accuracy of emotional faces recognition (Pedrosa Gil et al., 2009). Furthermore, our results revealed higher level of psychological distress in CD patients with especially pronounced symptoms of anxiety and depression. Discussing the relationship between the none motor disturbances and dystonia, the question arises whether these conditions develop independently in the clinical course or represent psychoreactive phenomena to this chronic and debilitating disease. It is being suggested that reduced cortical inhibition may play a role in primary dystonia (Ridding et al., 1995; Hummel et al., 2002) as well as in trait anxiety and depression (Wassermann et al., 2001) implying a possible common pathological background of these conditions. Jabusch et al. (2004) have also tried to disentangle this question with regard to anxiety in musicians with focal hand dystonia concluding that anxiety seem to precede the onset of the playing-related disorder. Similarly, other authors suggest that anxiety (Lauterbach et al., 2004; Jabusch et al., 2004) and depression (Heiman et al., 2004) may precede or develop independently of the clinical manifestations of dystonia and thus may not be considered as psychoreactive phenomena to a chronic and debilitating disease (Gundel et al., 2003; Heiman et al., 2004; Moraru et al., 2002).

Moreover, a number of studies of depression have found reduced metabolism in the basal ganglia (Baxter et al. , 1985; Buchsbaum, 1986 ; Mayberg et al. , 1994).. Additionally, in a study of depression resulting from stroke-related lesions (Morris et al. , 1996), 75% of patients with lesions to the left basal ganglia or left PFC were depressed, in contrast to only 21% of patients with lesions anywhere else in the brain. Furthermore, consistent with the hypothesis that the basal ganglia play an important role in positive emotional appraisal and experience (Canli et al., 1998; Lane et al. , 1997; Phillips et al., 1997) and that nonreactive forms of depression in most neuropsychological conditions arise from basal ganglia dysfunction it has been suggested that a basal ganglia damage might contribute to depression by impairing the ability to identify and appraise positive stimuli (Lieberman, 2000).

Concerning the personality profile of CD patients our findings designated specific personality features that appear to predominate in these patients. Evaluation of the individuality traits disclosed prominent psychosomatic complaints, accentuated strain and emotionality features in the patient group as well as less pronounced extroversion characteristics. This profile appears to be somehow characteristic to the patients suffering from cervical dystonia but it seems unrelated to the emotional processing deficit since the personality traits in CD did not correlate with the performance on emotional prosody recognition task. Moreover, there was no correlation with the severity, duration and age of dystonia onset suggesting that individuals with certain personality structure might be rather prone to develop dystonia instead of prominent personality features to evolve as a reaction to a chronic debilitating disease.

In conclusion, consistent with previous research findings on emotional prosody in other basal ganglia disorders, the present study disclosed a deficient emotional prosody perception in patients with primary cervical dystonia. Moreover, the discrimination of acoustic cues contributing to the classification of the emotional valence of affective prosody seems to be explicitly impaired. The displayed deficit involved all investigated emotional categories suggesting that the disturbed emotional prosody comprehension in CD is rather general in nature than restricted to certain discrete emotions. Furthermore, again in line with the literature, dystonia patients displayed more often anxiety, depression and some specific personality traits. Taken together these findings provide further evidence for the essential role of the basal ganglia in emotional prosody processing and also emphasize the importance to recognize the non-motor symptoms in patients with primary focal dystonia as complementary to the motor deficit.

References

- Alexander GE, Crutcher MD, DeLong MR. Basal ganglia-thalamocortical circuits: parallel substrates for motor, oculomotor, "prefrontal" and "limbic" functions. *Progress in brain research* 1990;85:119-146.
- Ariatti A, Benuzzi F, Nichelli P. Recognition of emotions from visual and prosodic cues in Parkinson's disease. *Neurol Sci* 2008;29:219-227.
- Bach DR, Grandjean D, Sander D, Herdener M, Strik WK, Seifritz E. The effect of appraisal level on processing of emotional prosody in meaningless speech. *NeuroImage* 2008;42:919-927.
- Baxter LR, Jr., Phelps ME, Mazziotta JC, Schwartz JM, Gerner RH, Selin CE, Sumida RM. Cerebral metabolic rates for glucose in mood disorders. Studies with positron emission tomography and fluorodeoxyglucose F 18. *Archives of general psychiatry* 1985;42:441-447.
- Berardelli A, Rothwell JC, Hallett M, Thompson PD, Manfredi M, Marsden CD. The pathophysiology of primary dystonia. *Brain* 1998;121 (Pt 7):1195-1212.
- Blair RJ, Morris JS, Frith CD, Perrett DI, Dolan RJ. Dissociable neural responses to facial expressions of sadness and anger. *Brain* 1999;122 (Pt 5):883-893.
- Blonder LX, Gur RE, Gur RC. The effects of right and left hemiparkinsonism on prosody. *Brain and language* 1989;36:193-207.
- Buchsbaum MS. Brain imaging in the search for biological markers in affective disorder. *The Journal of clinical psychiatry* 1986;47 Suppl:7-12.
- Calder AJ, Keane J, Lawrence AD, Manes F. Impaired recognition of anger following damage to the ventral striatum. *Brain* 2004;127:1958-1969.
- Cancelliere AE, Kertesz A. Lesion localization in acquired deficits of emotional expression and comprehension. *Brain and cognition* 1990;13:133-147.
- Canli T, Desmond JE, Zhao Z, Glover G, Gabrieli JD. Hemispheric asymmetry for emotional stimuli detected with fMRI. *Neuroreport* 1998;9:3233-3239.
- Crosson B. *Subcortical functions in language and memory*. Guilford Press: New York . 1992.
- Dara C, Monetta L, Pell MD. Vocal emotion processing in Parkinson's disease: reduced sensitivity to negative emotions. *Brain Res* 2008;1188:100-111.
- Defazio G, Berardelli A, Hallett M. Do primary adult-onset focal dystonias share aetiological factors? *Brain* 2007;130:1183-1193.
- Gundel H, Wolf A, Xidara V, Busch R, Ladwig KH, Jacobi F, von Rad M, Ceballos-Baumann AO. High psychiatric comorbidity in spasmodic torticollis: a controlled study. *The Journal of nervous and mental disease* 2003;191:465-473.
- Heiman GA, Ottman R, Saunders-Pullman RJ, Ozelius LJ, Risch NJ, Bressman SB. Increased risk for recurrent major depression in DYT1 dystonia mutation carriers. *Neurology* 2004;63:631-637.
- Hummel F, Andres F, Altenmuller E, Dichgans J, Gerloff C. Inhibitory control of acquired motor programmes in the human brain. *Brain* 2002;125:404-420.
- Jabusch HC, Muller SV, Altenmuller E. Anxiety in musicians with focal dystonia and those with chronic pain. *Mov Disord* 2004;19:1169-1175.

- Kotz SA, Meyer M, Alter K, Besson M, von Cramon DY, Friederici AD. On the lateralization of emotional prosody: an event-related functional MR investigation. *Brain and language* 2003;86:366-376.
- Lalande S, Braun CM, Charlebois N, Whitaker HA. Effects of right and left hemisphere cerebrovascular lesions on discrimination of prosodic and semantic aspects of affect in sentences. *Brain and language* 1992;42:165-186.
- Lane RD, Reiman EM, Ahern GL, Schwartz GE, Davidson RJ. Neuroanatomical correlates of happiness, sadness, and disgust. *The American journal of psychiatry* 1997;154:926-933.
- Lauterbach EC, Freeman A, Vogel RL. Differential DSM-III psychiatric disorder prevalence profiles in dystonia and Parkinson's disease. *The Journal of neuropsychiatry and clinical neurosciences* 2004;16:29-36.
- Lieberman MD. Intuition: a social cognitive neuroscience approach. *Psychological bulletin* 2000;126:109-137.
- Lloyd AJ. Comprehension of prosody in Parkinson's disease. *Cortex; a journal devoted to the study of the nervous system and behavior* 1999;35:389-402.
- Mayberg HS, Lewis PJ, Regenold W, Wagner HN, Jr. Paralimbic hypoperfusion in unipolar depression. *J Nucl Med* 1994;35:929-934.
- Miller KM, Okun MS, Fernandez HF, Jacobson CE, Rodriguez RL, Bowers D. Depression symptoms in movement disorders: comparing Parkinson's disease, dystonia, and essential tremor. *Mov Disord* 2007;22:666-672.
- Moraru E, Schnider P, Wimmer A, Wenzel T, Birner P, Griengl H, Auff E. Relation between depression and anxiety in dystonic patients: implications for clinical management. *Depression and anxiety* 2002;16:100-103.
- Morris PL, Robinson RG, Raphael B, Hopwood MJ. Lesion location and poststroke depression. *The Journal of neuropsychiatry and clinical neurosciences* 1996;8:399-403.
- Paulmann S, Pell MD, Kotz SA. Functional contributions of the basal ganglia to emotional prosody: evidence from ERPs. *Brain Res* 2008;1217:171-178.
- Pedrosa Gil F, Ridout N, Kessler H, Neuffer M, Schoechlin C, Traue HC, Nickel M. Facial emotion recognition and alexithymia in adults with somatoform disorders. *Depression and anxiety* 2009;26:E26-33.
- Pell MD. On the receptive prosodic loss in Parkinson's disease. *Cortex; a journal devoted to the study of the nervous system and behavior* 1996;32:693-704.
- Phillips ML, Young AW, Senior C, Brammer M, Andrew C, Calder AJ, Bullmore ET, Perrett DI, Rowland D, Williams SC, Gray JA, David AS. A specific neural substrate for perceiving facial expressions of disgust. *Nature* 1997;389:495-498.
- Ridding MC, Sheean G, Rothwell JC, Inzelberg R, Kujirai T. Changes in the balance between motor cortical excitation and inhibition in focal, task specific dystonia. *Journal of neurology, neurosurgery, and psychiatry* 1995;59:493-498.
- Scherer KR, Banse R, . HGW, Goldbeck T. Vocal cues in emotion encoding and decoding. *Motiv. Emot.* 1991; 15 (2), 123-148.
- Schroder C, Mobes J, Schutze M, Szymanowski F, Nager W, Bangert M, Munte TF, Dengler R. Perception of emotional speech in Parkinson's disease. *Mov Disord* 2006;21:1774-1778.
- Speedie LJ, Brake N, Folstein SE, Bowers D, Heilman KM. Comprehension of prosody in Huntington's disease. *Journal of neurology, neurosurgery, and psychiatry* 1990;53:607-610.
- Sprengelmeyer R, Rausch M, Eysel UT, Przuntek H. Neural structures associated with recognition of facial expressions of basic emotions. *Proceedings* 1998;265:1927-1931.
- Sprengelmeyer R, Young AW, Calder AJ, Karnat A, Lange H, Homberg V, Perrett DI, Rowland D. Loss of disgust. Perception of faces and emotions in Huntington's disease. *Brain* 1996;119 (Pt 5):1647-1665.

- Wassermann EM, Greenberg BD, Nguyen MB, Murphy DL. Motor cortex excitability correlates with an anxiety-related personality trait. *Biological psychiatry* 2001;50:377-382.
- Weddell RA. Effects of subcortical lesion site on human emotional behavior. *Brain and cognition* 1994;25:161-193.
- Wildgruber D, Pihan H, Ackermann H, Erb M, Grodd W. Dynamic brain activation during processing of emotional intonation: influence of acoustic parameters, emotional valence, and sex. *NeuroImage* 2002;15:856-869.
- Yip JT, Lee TM, Ho SL, Tsang KL, Li LS. Emotion recognition in patients with idiopathic Parkinson's disease. *Mov Disord* 2003;18:1115-1122.

Acknowledgements

First I would like to thank my main supervisor Prof. Reinhard Dengler for giving me the opportunity to carry out this project and conduct the experimental work at his department. He provided his constant support, encouragement and guidance through the obstacles emerging in the course of my PhD studies. Without his help during the implementation of the project this dissertation would not have been possible.

I extend my appreciations to my co-supervisors, Prof. Eckart Altenmueller and Prof. Elke Zimmermann for their critical comments, new ideas and valuable advices for improving my work.

I would like to thank as well to Dr. Christine Schroeder for her scientific guidance and constant support during my PhD study and especially for the late nights and weekends spent in providing feedback on my publications.

My thanks extend to Prof. Wolfgang Baumgartner for his fair and open approach in leading the PhD program and to Dr. Dagmar Esser and Mrs. Nadja Borsum for their help in my first days in Germany and permanent assistance during the course of my PhD studies.

My gratitude goes also to my colleagues from the Department of Neurology for their collegial support and friendship and especially to Milan Arsic, Danela Ragancokova, Paraskevi Kotsoudaki and Jelena Skuljec, who had volunteered to be my subjects

Acknowledgements

when I needed to test my paradigm. I thank also to Anja Fellbrich for helping me with recruitment of the subjects that participated in this experiment and J. Kilian and Andreas Niesel for the technical assistance that they provided during the whole period of my experimental work.

I give my special thanks to my family, my parents Rada and Tashko and my brother Nikolay for their unconditional love, understanding and support, for believing in me and constantly encouraging me in pursuing my goals.

Last, but not the least, I thank to all those that I could not mention here, but who were, at least in my thoughts and all the time with me.

This work was supported by Marie Curie Early Stage Training Fellowship (EST) of the European Community's Sixth Framework Programme under contract number MEST-CT-2005-021014.