Behavioral and neuroimaging studies on language processing in Dutch speakers with Parkinson's disease
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1.1 Parkinson’s disease

Parkinson’s disease, from now on referred to as PD, was named after James Parkinson (1755-1824), who was the first to describe the disease in 1817 in *An Essay on the Shaking Palsy*. PD is one of the most common progressive degenerative neurological diseases in elderly people, but the cause is still not known. In the European community, PD is equally present in men and women of 50 years of age or older and has a prevalence of 1.6 per 1000 persons (de Rijk et al., 1997). A recent study found that the incidence rates for PD increase from .3 per 1000 persons per year in subjects aged 55 to 65 years, to 4.4 per 1000 persons per year for subjects aged 85 years and older (de Lau et al., 2004).

The diagnosis of PD is clinical, based on the presence of at least two of the three major motor symptoms: resting tremor, rigidity, and akinesia/bradykinesia\(^1\) (Levy & Cummings, 1999). Typically, PD has an asymmetrical onset of these motor symptoms and is additionally characterized by a breakdown in walking skills and maintaining upright balance. Secondary motor symptoms may also be present and include: freezing, reduced eyelid blink rate, masked face, dysarthria, hypophonia, dysphagia, sialorrhoea, micrographia and many more (Jankovic, 2008; Leenders, 2002). Clinical observations show that secondary speech motor symptoms, such as dysarthria and hypophonia, are experienced as equally or even more disabling than the cardinal features of PD.

The hypokinetic dysarthria described in patients with PD is characterized by monotonous, soft and breathy speech with variable rate (Canter, 1965; Darley, Aronson, & Brown, 1975; for an extensive review see Pinto et al., 2004).

In clinical practice, two scales are frequently used for the diagnosis of PD. Both scales were used in the studies described in this thesis. First, the Hoehn and Yahr scale (H&Y scale, Hoehn & Yahr, 1967), is one of the earliest severity scales and is a rough evaluation of the severity of parkinsonian symptoms (see Appendix A for a modified version of the H&Y scale). Second, the Unified Parkinson’s Disease Rating scale (UPDRS, Fahn et al., 1987), which assesses disability and impairment in PD in different domains. In the research described in this thesis, only motor part III was used (see Appendix B).

Non-motor symptoms mainly comprise cognitive dysfunction/dementia, autonomic disturbances, depression, and psychotic symptoms. The prevalence of dementia in PD increases in relation to disease duration (Aarsland, Andersen, Larsen, & Lolk, 2003) and has a

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\(^1\) Akinesia is the inability to initiate movement. Bradykinesia is the "reduced speed of movement of a muscle through its range" (Love & Webb, 1992). Hypokinesia is the decrease of amplitude of movements.
destructive impact on the patient’s life and that of his environment. The subcortical dementia that often occurs in the final stages of PD is different from cortical dementias such as Alzheimer’s dementia (AD). Unlike in AD, dementia in PD exhibits normal or only slightly decreased performance in gnosia and praxis functions, and is typically characterized by a progressive dysexecutive syndrome with disturbed memory functions and attention (Dubois & Pillon, 1997). Dementia in PD is often, but not always, accompanied by hallucinations and delusions (Bosboom, Stoffers, & Wolters, 2004). In the language domain, demented PD patients show reduced verbal fluency, poor confrontation naming abilities, decreased word list generation, and difficulties in word-finding (Dubois & Pillon, 1997; Pahwa, et al., 1998). Impaired verbal fluency is the main language deficit in demented PD patients and is more severe in them than in AD patients (Emre, 2003).

PD patients with dementia were excluded from participation in the experiments described in this thesis. We focused exclusively on the impairments of cognition, including language processing in PD patients in whom overt dementia was not present. Impairments of non-demented PD patients in different cognitive domains are the topic of this thesis. Executive functions and memory will be discussed in Chapter 2 and language processing in Chapter 3.

1.2 Linguistic background

In the following section I will introduce the linguistic background of the different experiments described in this thesis.

Language is a higher cognitive function in which linear sequencing is inherently present as shown at multiple structural dimensions: in phonology, morphology, syntax and discourse. In classic linguistic theories favoring Noam Chomsky’s ideas, but also in most psycholinguistic models, language is seen as a dual system in which morphological and lexical information is retrieved from declarative memory (i.e., the mental lexicon). This information is assembled into larger structures (i.e., phrases, clauses) according to procedural rules employed by the mental grammar (Chomsky, 1981, 1995, 1998; Jackendoff, 2002, 2007; Pinker, 1999; Pinker & Jackendoff, 2005; Pinker & Ullman, 2002; Ullman, 2001, 2004).

Word order

The rules of grammar specify the sequential order of words in a sentence. These rules make, for example, sentence (1) acceptable in Dutch and sentence (2) ungrammatical:

(1) Jan kust Marie
    ‘John kisses Mary’

(2) *Jan Marie kust
    ‘* John Mary kisses’

The order of the words in the Dutch sentence ‘Jan kust Marie’ (1) encodes ‘who did what to whom’.

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2 Following the conventions of theoretical linguistics, anomalous sentences are preceded with an asterisk.
Base word order in Dutch is Subject-Object-Verb (SOV). Finite verbs in subordinate clauses (3) and non-finite verbs (i.e., infinitives and participles) in main clauses (4) are in base position. There is a grammatical rule, linguistically known as Verb Second that postulates that in the main clause the finite verb should be in second position (see sentence 1).

(3) Jan die Marie kust
   ‘John who Mary kisses’
   (John who is kissing Mary)

(4) Jan heeft Marie gekust
   ‘John has Mary kissed’
   (John has kissed Mary)

In derived order sentences, such as object-relatives, the sentence components are not in their base position. Consider the Dutch object-relative in (5) as an example of a derived order sentence:

(5) De appels, die de kinderen plukken t, zijn rot
   ‘The apples that the children picked are rotten’

In object-relatives, the relationship between word order and grammatical roles is derived: the grammatical object precedes the subject. But not only the grammatical roles are in derived order. The thematic roles are too. In (5) ‘children’ are agent and ‘apples’ are theme. In base order sentences, the agent usually precedes the theme.

The following are examples of an active (6a) and a passive (6b) in Dutch:

(6a) De kinderen plukken de appels
    ‘The children pick the apples’

(6b) De appels, worden door de kinderen t, geplukt
    ‘The apples are by the children picked’

In passive constructions, the grammatical roles are in base order. In sentence (6b) the subject (‘the apples’) precedes the finite verb (‘are’) which precedes the prepositional phrase (‘by the children’). However, the thematic roles are not in their base position. The theme (‘apples’) is subject of the sentence and, thus, precedes the finite verb. The agent (‘children’) follows the finite verb.

In sum, in the object relative sentence in (5) the object with the theme role precedes the subject with the agent role. So both the grammatical and the thematic roles are in derived position. In passives, like in (6b), the grammatical roles are in base position (S-Vfin-PP-V), but the thematic roles are in derived position, that is, the theme is preceding the agent.

To summarize, in Dutch the base word order is considered to be SOV. All other word orders are derived from this template.
Verb agreement
Like in most Indo-European languages, in Dutch the finite verb agrees in number and person with the subject. The inflectional features of sentences are demonstrated by comparing the meaning of sentence (7a) with the meaning of sentence (7b):

(7a) De jongen kust het meisje
   ‘The boy kisses the girl’
(7b) De jongens kussen het meisje
   ‘The boys kiss the girl’

Tense
As shown by the Dutch sentences in (8), the finite verb is also inflected for Tense. In sentence (8a) the finite verb is in present tense, while in sentence (8b) the finite verb is in past tense.

(8a) De jongen kust het meisje
    ‘The boy kisses the girl’
(8b) De jongen kuste het meisje
    ‘The boy kissed the girl’

More grammatical features of the verb
It is generally assumed that the semantic and syntactic features of the verb determine sentence structure (Shapiro, Zurif, & Grimshaw, 1987; Collina, Marangolo, & Tabossi, 2001; Van Valin 2001). Verbs are crucial to both comprehension and production of sentences, since verbs specify the relations between the entities in the sentence. For example, the verb provides information about (1) the number of entities participating in the event described by the verb (argument structure), (2) the syntactic types of phrases that can complement the verb (subcategorization frame) and (3) the semantic (thematic) roles of the complements of the verb.

In this thesis, we investigate the effects of these grammatical features (word order, verbs and their inflections) described on comprehension and production of Dutch-speaking PD patients. The results are reported in four research chapters.
1.3 Overview thesis

This thesis focuses on the underlying cause of the language impairments in PD patients and more in particular on the influence of impaired executive functions on language processing. PD patients, who all have dysfunctional cortico-striato-cortical circuits, were studied to evidence the implication of these circuits in sequential language processing.

Chapters 2, 3 and 6 provide the theoretical background to the pathology and clinical symptomatology of PD, the language deficits and functional neuro-imaging studies in PD patients respectively.

One of the four research chapters in this thesis is presented in the original form, as it was accepted for publication in Cortex. Chapters 4 and 5 consist of two behavioral studies covering the influence of executive functions on verb production in sentence context and sentence comprehension in patients with PD. Chapter 7 describes a functional Magnetic Resonance Imaging (fMRI) experiment on the involvement of the basal ganglia (BG) and the inferior frontal gyrus (IFG), both subparts of the cortico-striato-cortical circuits, in processing written sentence materials in healthy participants. In the fMRI study the variables of ‘word order’ (active vs. passive voice) and ‘grammaticality’ (no violation, inflectional violation vs. verb-argument structure violation) were factorially manipulated. Chapter 8 centers on the involvement of the BG and the IFG, shown to be active in an fMRI study in patients with PD compared to age- and education-matched healthy control participants.

Finally, in Chapter 9 the results of the four empirical studies will be discussed and this book will be concluded with suggestions for future research.

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3 Chapters 5, 7 and 8 will be adjusted to article format to be submitted for publication. Chapter 3 and Chapter 6 will be combined into one chapter that will be a part of an open access book on Parkinson’ disease (working title).