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The Portuguese Version of the Dutch Linguistic Intraoperative Protocol: Semantic tasks

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Dissertação apresentada à Universidade de Aveiro para cumprimento dos requisitos necessários à obtenção do grau de Mestre em Terapia da Fala, realizada sob a orientação científica do Professor Doutor Luís Miguel Teixeira de Jesus, Professor Coordenador com Agregação da Universidade de Aveiro.

“We die. That may be the meaning of life. But we do language. That may be the measure of our lives.”

— Toni Morrison

O júri

Presidente	Professora Doutora Marisa Lobo Lousada Professora Adjunta da Universidade de Aveiro
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Palavras-chave Cirurgia com o paciente acordado; Mapeamento cerebral; Gliomas de baixo grau; Avaliação da Linguagem; Semântica

Resumo

Enquadramento: O Dutch Linguistic Intraoperative Protocol (DuLIP) é uma bateria de testes que permite avaliar a linguagem no pré, intra e pós-operatório de pacientes com gliomas de baixo grau. O paciente está acordado durante a cirurgia o que permite o mapeamento cerebral usando a estimulação elétrica direta. A versão portuguesa do DuLIP (DuLIP-PE) contempla tarefas de fonologia, sintaxe, semântica, nomeação e articulação. Esta Dissertação foca-se na área da semântica e nas suas oito tarefas.

Objetivos: Traduzir e adaptar as tarefas de semântica do DuLIP para o Português Europeu.

Métodos: Foi realizado um estudo qualitativo e quantitativo, de forma a traduzir e adaptar o DuLIP e este foi aplicado à população normal, de forma a obter dados normativos. Foram seguidas as indicações dos autores originais. Para cada tarefa de semântica, características como a frequência, idade de aquisição, imaginabilidade, prevalência, comprimento e categoria semântica da palavra foram tidas em conta. O Protocolo foi administrado a 144 participantes adultos e saudáveis, que satisfazessem os critérios de inclusão.

Resultados: Em algumas tarefas de semântica foram eliminados itens que não atingiram 90% de respostas certas dadas pelos participantes. Participaram no estudo 82 mulheres e 62 homens, com idades compreendidas entre os 18 e os 89 anos e com 4 a 24 anos de escolaridade. Foi possível observar que as mulheres obtiveram melhores resultados, não existindo diferenças estatisticamente significativas entre homens e mulheres ($p \le 0.0024$). Quanto menor a idade, melhores os resultados, existindo diferenças estatisticamente significativas em 5 provas de semântica. Relativamente à escolaridade quanto maior número de anos de escolaridade melhores os resultados, com diferenças significativas em 5 tarefas ($p \le 0.0024$). Observou-se uma correlação moderada ($r=0.410$) entre a capacidade cognitiva e a tarefa da palavra intrusa.

Conclusão: Realizou-se a tradução e adaptação das tarefas de semântica do DuLIP, sendo esta bateria de testes essencial para a avaliação da linguagem no contexto de neurocirurgia, aumentando o tempo de vida do utente, a sua qualidade de vida e a minimização de sequelas no pós-operatório.

Keywords Awake brain surgery; Brain Mapping; Low-Grade Gliomas; Language Assessment; Semantics

Abstract

Background: The Dutch Linguistic Intraoperative Protocol (DuLIP) is a battery of tests that allows the language evaluation in pre, intra and postoperative of patients with low grade gliomas. The patient is awake during surgery which allows brain mapping using direct electrical stimulation. The Portuguese version of DuLIP (DuLIP-EP) includes phonology, syntax, semantics, naming and articulation tasks. This Dissertation focuses on the eight semantics tasks.

Aim: Translate and adapt DuLIP semantic tasks to European Portuguese.

Methods: A qualitative and quantitative study was performed to translate and adapt DuLIP, which was then used to assess a group of normal participants in order to obtain normative data. The instructions of the original authors were followed. For each semantic task characteristics such as frequency, age of acquisition, imaginability, prevalence, length and semantic category of the word were considered. The DuLIP was administered to 144 healthy adult participants who met the inclusion criteria.

Results: Some of the items in the semantic tasks were eliminated as they did not reach 90% of right answers given by participants. The total 82 women and 62 men, aged between 18 and 89 years and with 4 to 24 years of education, participated in the study. It was observed that women obtained better results, with no statistically significant differences between men and women ($p \leq 0.0024$). The younger the better the results, and there were statistically significant differences in 5 semantic tests. Regarding education, the higher the number of years of education the better the scores, with significant differences in 5 tasks ($p \leq 0.0024$). A moderate correlation ($r = 0.410$) was observed between cognitive ability and the results of the intrusive word task.

Conclusion: The DuLIP-EP semantic tasks were translated and adapted, resulting in a battery of tests that is essential for language evaluation in the context of neurosurgery, increasing the patient's lifetime, quality of life and decreasing the postoperative sequalae.

Abbreviations and/or acronyms

DuLIP - Dutch Linguistic Intraoperative Protocol

LGG - Low-Grade Gliomas

DES - Direct Electrical Stimulation

EP - European Portuguese

IFC - Inferior Frontal Córtex

ILF - Inferior Longitudinal Fascicle

UF - Uncinate Fascicle

IFOF - Inferior Fronto-Occipital Fascicle

DuLIP-EP - Dutch Linguistic Intraoperative Protocol – European – Portuguese

CRPC - Contemporary Portuguese Reference Corpus

MMSE - Mini Mental State Examination

ACE III - Addenbrooke's Cognitive Examination III

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1. Introduction

A team of researchers from the Netherlands has developed a protocol – the Dutch Linguistic Intraoperative Protocol (DuLIP) – which allows pre, intra and postoperative assessment of language skills in patients with brain tumors, specifically low-grade gliomas (LGG). These patients are awake during this procedure which allows brain mapping by using Direct Electrical Stimulation (DES). This technique is currently considered a benchmark to identify eloquent cortical and subcortical structures and to improve the quality of the patient's life (Coello et al., 2013; Witte et al., 2015).

The DuLIP includes semantic, syntax, phonology, and articulation tasks. These tasks are applied considering the location of the tumor and its functional networks since there are specific anatomical-function connections. This set of linguistic tools contains one object naming test, four phonological tests, eight semantic tests, five syntactic tests and one articulatory test (Witte et al., 2015) .

The DuLIP has already been adapted to languages such as Spanish and Italian. There was a need to translate, culturally adapt and validate the protocol into European Portuguese (EP), due to the lack of instruments to appraise language during this type of surgery in Portugal. Therefore 144 neurologically healthy adults participated in the normative study.

This Dissertation focuses on semantic-related tasks and, therefore, refers to the whole process of translation and adaptation into EP.

This study aims to investigate if: there are significant differences between gender; there are significant differences across age groups; there are significant differences according to years of education; the cognitive results influence semantics.

1.1. Language

"Language is communication through use of symbols and is unique to humans" (Gill & Damann, 2015, p. 627). Language requires several cognitive processes, since it is a complex brain function that may be affected by brain damage (Gill & Damann, 2015).

Language does not only fit into the gray matter of the frontal and temporal cortex, but also into the pathways that interconnect these regions. Whenever there are injuries in these pathways, language processing is affected, highlighting their importance (Friederici, 2009).

1.2. Semantics

Through semantic processing it is possible to access the meaning of words, objects, people and facts, which is a uniquely human ability (Moritz-Gasser, Herbet, & Duffau, 2013).

Understanding of semantic organisation is possible through neurofunctional imaging methods, allowing the identification of some brain regions responsible for the cortical organisation of the semantic system (Duffau et al., 2005).

Many authors have conducted research to better understand semantic organisation and its storage (Baldo, SChwartz, Wilkins, & Dronkers, 2006; Bello et al., 2007, 2008; Bertani et al., 2009; Coello et al., 2013; Witte et al., 2015; Rofes, 2015; Duffau et al., 2005; Friederici, 2009; Gill & Damann, 2015; Huth, Heer, Griffiths, Theunissen, & Gallant, 2016; Lubrano, Filleron, Démonet, & Roux, 2014; Moritz-Gasser, Herbet, & Duffau 2013; Patterson, Nestor, & Rogers, 2007; Richardson, Seghier, Leff, Thomas, & Price, 2011).

Semantic information is stored in networks constituting the semantic memory. Several studies have focused on the cortical organisation of semantic processing, pointing out that there is a large-scale network throughout the brain, involving the frontal, temporal and parietal lobes. Some researchers, in different studies, describe two areas in the left hemisphere as having utmost importance (Duffau et al., 2005): The left posterior temporal regions and the left inferior frontal cortex (IFC).

It is in the left temporal lobe that the semantic content is contained and organised. During comprehension tasks, whether visual, oral or somesthetic, the regions of the posterior part of the superior temporal lobe are activated. Tasks such as reading or naming (visual tasks) can incorporate the basal inferior temporal areas related to lexical retrieval. Regarding the semantic role of IFC, more specifically pars orbitalis, pars triangularis (inferior and anterior) and the dorsolateral prefrontal cortex may be related to the executive aspects of semantic processing and the pars opercularis (posterior area) is more involved in syntactic task (Duffau et al., 2005).

There are more data about this cortical network organisation, but still, there is a lack of clear information about subcortical links related to semantics and about the anatomo-functional connectivity subjacent to the semantic system (Duffau et al., 2005).

It has been suggested that there are different white matter pathways to connect different semantic-related brain areas, such as the Inferior Longitudinal Fascicle (ILF) and Uncinate Fascicle (UF), the extreme capsule, and the Inferior Fronto-Occipital Fascicle (IFOF) (Bertani et al., 2009; Moritz-Gasser et al., 2013).

Moritz-Gasser et al. (2013) concluded that the use of subcortical mapping demonstrates that the left IFOF, after electrical stimulation, caused semantic disfunction, thus the IFOF is indispensable regarding the semantic processing and no other subcortical fascicles replaces it.

The results of the study refer the existence of two important pathways in semantics: one direct, which will be IFOF, and one indirect, possibly the ILF and UF, distinguishing only the different meanings in semantic processing (Moritz-Gasser & Duffau, 2013).

The difference between these two pathways relates to semantic processing. For it has been observed after DES stimulation that semantic disturbances (semantic paraphasias) occur during IFOF stimulation, indicating that this direct pathway is crucial and unique in semantic processing as there is no subcortical fascicle capable of performing its functions or replacing it. Therefore, it is suggested that it is this fascicle that distinguishes humans from other beings, as it allows to generate and understand language, to work concepts, to capture and understand the surrounding world (Moritz-Gasser et al., 2013).

1.3. Awake brain surgery

The Dutch Linguistic Intraoperative Protocol is used with patients with low-grade gliomas during neurosurgeries when DES is performed to allow subcortical mapping.

The primary goals of neurosurgery are related to increasing the patient's life expectancy by preserving and improving their quality of life by minimising the risk of sequelae on the patient. It must be performed within specific functional and anatomical limits (Bertani et al., 2009; H. Duffau, 2007), because it is necessary to resect the tumour as much as possible and concomitantly obtain the best possible functional result (Coello et al., 2013). The objective is to maximise the chances the patient has to return to his daily life, reintegrating society both personally and professionally. These factors are extremely important since most patients with this condition are still quite young. During surgery and using brain mapping techniques, it is possible to identify and preserve eloquent brain areas, which are related to motor, language, memory and visuospatial functions (Bertani et al., 2009).

In order to improve surgical planning before and during surgery, there are several functional imaging approaches that allow better localisation of the tumour (Bello et al., 2008). Usually, LGG occur in eloquent brain areas and involve cortical and subcortical areas, being an extremely invasive tumour that can cause language disorders (Bello et al., 2007). These types of intrinsic tumours eventually progress to malignancy and slowly infiltrate the brain (Bertani et al., 2009). The most common treatment is resection, but this requires the detailed preoperative assessment by a multidisciplinary team, composed of neurosurgeons, neuropsychologists, and neurophysiologists, to jointly define the location, and extent of the lesion. It should be noted that each tumour causes specific changes in the brain and life of the patient, so the clinical signs and symptoms are highly variable depending on the individual (Bertani et al., 2009). Each treatment has to take into account the characteristics of the tumour and the patient (Bertani et al., 2009).

At the outset it will be possible to achieve this goal in one surgery, but additional surgeries may be required. In order to preserve brain areas involved in motor, language, memory and visuospatial functions, brain mapping techniques are performed. This being a very complex approach requires extensive training from a dedicated and capable team (Bertani et al., 2009).

In order to identify functional language tracts, subcortical stimulation is also used during LGG resection, reducing morbidity and increasing resection quality (Bello et al., 2007). Bello et al.

(2007, p. 68) conclude that "subcortical mapping requires stimulation to be alternated with resection, in a back-and-forth fashion".

During surgery and glioma resection subcortical stimulation is used to identify subcortical language-related areas. This has been successful in LGG involving speech areas. If the tumour involves the language areas, the patient will have to wake up during surgery so that the tumour resection can be evaluated with a language assessment protocol. Considering the limited time and patient's position imposed by the surgery, language subcortical mapping may be difficult to perform (Bello et al., 2007). Resection is interrupted whenever approaching the cortical and subcortical areas of language, motor control and visuospatial perception, since the purpose of mapping is to identify and preserve these same areas (Bertani et al., 2009).

During LGG surgery, DES is considered a gold standard since it allows the identification and preservation of the most important brain areas. If they are removed, there is a risk of causing irreversible neurological deficits. After preoperative evaluation by each specialised health professional, the patient is carefully monitored and followed up, taking into account the anaesthesia, neuropsychological and the functional and anatomical imaging examination (Bertani et al., 2009).

In order to perform cortical and subcortical mapping it is necessary to use DES which is a bipolar manual stimulator that provides biphasic square wave pulses. To evoke motor responses, the intensity of stimulation ranges from 2 to 8 mA. When the right and proper intensity is determined, it is used throughout the surgical procedure. This brain mapping is performed by alternating resection with stimulation, so it is possible to test motor, language and cognitive function. The duration of the stimulus is about 4 s (Bertani et al., 2009).

The presence of a Speech and Language Therapist during surgery is crucial, as he/she will be the one, during the awake period, that will perform and apply various language tests. The Speech and Language Therapist will assess the spontaneous production of speech and language, and will also test the identification of the cortical and subcortical brain areas inherent to these tasks, specifying if any language disturbance occurred during resection (Bello et al., 2007). The patient may produce some errors whenever the areas of speech are stimulated. This language disturbance can occur during stimulation but also without it and can be of various types (Bertani et al., 2009).

Resection is always interrupted when eloquent brain areas are found. By preserving these areas, the patient will have the minimum permanent postoperative deficits, which will contribute to extending their life and improving their quality of life. It is known that brain mapping is a very demanding technique, which is why a qualified and professional team is required, in close cooperation between the different professionals (Bertani et al., 2009).

2. Method

In order to translate and adapt DuLIP we had first to translate and culturally adapt the battery of tests and second to apply it to the Portuguese normal population in order to obtain normative data.

2.1. Translation and adaption

Regarding adaptation, specific instructions of the original authors were followed: At first a literal translation of the original tool, trying to keep as many stimuli as those used in the DuLIP original study as possible. All the tasks had to follow some specific features and variables.

The Portuguese version of DuLIP (DuLIP-EP) includes phonological, syntactic, semantic, naming and articulatory tests, but this Dissertation is only focused in the semantics tasks. All items were carefully chosen considering the original study. Some specific characteristics will be presented below.

The frequency of a word is related to the number of times that word is used by speakers (Leitão, Figueira, & De Almeida, 2014; Monsell, Doyle, & Haggard, 1989). High frequency words are known to more people and are processed quicker than low frequency words. Word frequency is important for memory performance and semantic decision (Brysbaert, Mandera, & Keuleers, 2018).

Frequency could be accessed using the Contemporary Portuguese Reference Corpus (CRPC), which is a huge electronic corpus of the EP, containing entries from about 291 311 212 words in written texts and from transcriptions of oral recordings (CLUL, 2013).

Imaginability, another factor that could have been considered in DuLIP-EP, refers to the ease with which a word evokes an experience. That is, any words that relate to any sense-related experience will increase the imaginability (Leitão et al., 2014). It was not possible to evaluate this variable because a corpus for EP was not found.

Age of acquisition refers to the age at which the word was learned (Leitão et al., 2014). These values were found for some words in the study by Ventura et al. (2014).

Word prevalence, defined as word awareness in the population (Brysbaert, Stevens, Mandera, & Keuleers, 2016), also could not be considered in our work, since a corpus for EP was not accessible.

Given these specificities, each task had to be analysed using the indicators discussed sections 2.1.1. to 2.1.6.

All items were discussed by the M.Sc. student and the original DuLIP authors, particularly when uncertainties regarding translation and adaptation come up, until a consensus was found.

2.1.1. Reading with semantic odd word out

In this test it was considered pertinent to keep the words used in the original study. However, some words were changed, in order to culturally adapt the items to the Portuguese population, but always keeping their semantic category. For example, one of the words used in the original test was <*quivi*> (<kiwi>), but it was decided to exchange this fruit for <*melão*> (<melon>) because the orthography could be confusing. In the beverage category, a well-known brand of soda for <*sumo*> (<juice>) was changed due to copyright issues. In the category of birds, a bird known in the Netherlands (<vink>) was changed to <*pomba*> (<dove>), as this bird is not very common in Portugal. With regard to the category of trees, <*faia*> (<beech tree>) was changed to <*castanheiro*> (<chestnut tree>), for this word in Portuguese is more usual (CLUL, 2013). In the category of insects <*besouro*> (<beetle>) was changed to <*joaninha*> (<ladybug>), because it is more frequent and therefore more used in Portuguese (Brysbaert et al., 2018, 2016; CLUL, 2013; Monsell et al., 1989). Data regarding word length, frequency, age of acquisition and word category were considered as in the original study.

The participants must read aloud the word that doesn't fit semantically a list of 4 words (25 items). With this test it is possible to evaluate the semantic judgement via the lexical visual input route, as well as reading, verbal semantic knowledge and semantic processing. By stimulating the temporal (posterior and superior), the prefrontal (orbitofrontal and dorsolateral) regions (Duffau et al., 2005), the parietal regions (Roux et al., 2004) and the occipital regions (Gras-Combe, Moritz-Gasser, Herbet, & Duffau, 2012) all those functions mentioned previously may be distorted. A disruption of semantic judgment (Bello et al., 2007; Duffau et al., 2005; Moritz-Gasser et al., 2013) may occur by stimulating the UF, the ILF (Bello et al., 2007), and the IFOF, at the subcortical level (Witte et al., 2015) (Fig 1A).

livro mar revista jornal **A**	 **B**	padeiro talhante … **C**
Eu lavo as minhas mãos com… **D**	O gato está a vestir roupa. **E**	Na escola… **F**

Figure 1. Semantic tasks: (A) Reading with semantic odd word out. The target is <*mar*> (<sea>) because it’s not semantically related to the other three words; (B) Reading with semantic odd picture out. The target is <*telefone*> (<telephone>) because it’s not semantically related to the other two images; (C) Semantic association. The target item can be <*florista*> (<florist>) or <*advogado*> (<lawyer>) or any other word semantically related within the same category; (D) Sentence completion (closed context). A possible target answer can be <*sabão*> (<soap>) <*Eu lavo as mãos com sabão*> (<I wash my hands with soap>). An incorrect answer can be <*tinta*> (<ink>) (<I wash my hands with ink>). (E) Semantic sentence judgment. The correct answer is <*não*> (<no>), because this sentence is semantically wrong. (F) Sentence completion (broad context). A possible target answer can be <*aprendi a ler*> (<I learned to read>).

2.1.2. Naming with semantic odd picture out

Since this is a test with images, Snodgrass and Vanderwart's (1980) open access database was used, as in the original study, considering the study by Ventura et al. (2014) in a Portuguese population (Witte et al., 2015; Snodgrass & Vanderwart, 1980; Ventura, 2014). These are black and white images with a simple trace, which can be easily and quickly identified (Biederman & Ju, 1988). It was taken into consideration aspects such frequency, age of acquisition, word category and the target words should be named within 4 s, because of the DES limited time (Witte et al., 2015).

It was not possible to keep all the images used in the original study because 16 entities are not easily framed into one category and were therefore removed from the study and 41 had been eliminated because the consensus among the participants was less than 60% (Ventura, 2014). For this reason, 23 images had to be removed from the DuLIP-EP and exchanged for others validated for EP (Ventura et al. 2014). Whenever possible, some pictures were replaced for images with the same semantic category, but in order not to repeat stimuli, it was sometimes necessary to use other categories. However, the original authors did not find any inconvenience in these changes. Action pictures were also rejected because they were not considered in the study by Ventura (2014).

Participants have to name the picture that doesn't fit semantically in a group of 3 black and white drawings (25 items) (Witte et al., 2015). The purpose of this task is to evaluate non-verbal semantic judgment and naming. Just as in the task of semantic odd word out, semantic knowledge and processing are evaluated but, instead of written words, pictures are used (Snodgrass & Vanderwart, 1980; Ventura, 2014). This test stimulates temporal, prefrontal regions, IFOF and the ILF (Moritz-Gasser et al., 2013) (Fig 1B).

2.1.3. Semantic association task

For this task, a literal translation was performed, but it was necessary to change some items, always maintaining their semantic category. Eight units have been changed to be more common words in Portuguese. An example of this type of changes is <*abeto*> (<fri tree>) for <*pinheiro*> (<chestnut tree>), since the latter is more frequent in EP (CLUL, 2013).

Participants should read two words and add a third semantically linked to the previous ones (25 items) (Witte et al., 2015). The goal of this test is to analyse the lexical-semantic processing and also for assessing reading, semantic knowledge and producing words according to a specified concept (Witte et al., 2015). It's important in posterior and frontal brain regions and to map the IFOF (Coello et al., 2013) (Fig 1C).

2.1.4. Sentence completion (closed context)

In this task it is possible to maintain sentence structure and verb tenses. It was only necessary to change the Dutch proper names to Portuguese ones.

The participants have to read and correctly complete sentences in a meaningful way- syntactically and semantically, in order to assess speech, reading and language dynamics (25 items) (Witte et al., 2015). By stimulating the supplementary motor area, Broca's area, the insula, the subcallosal fascicle and the ILF (Bello et al., 2007) there is a reduction of spontaneous speech (Fontaine, Capelle, & Duffau, 2002) (Fig. 1D).

2.1.5. Judgment of semantically anomalous and correct sentences (semantic sentence judgment)

For this test all the criteria were kept: Passive/active voice, time/verbal mode and sentence type.

The goal of this task is to discriminate between semantically correct and incorrect sentences (50 items) (Witte et al., 2015). It allows the evaluation of the auditory input route, semantic awareness, knowledge and comprehension and it's used for temporal cortical and subcortical areas (Bello et al., 2007; Bertani et al., 2009; Pereira et al., 2009; Santini et al., 2012) (Fig. 1E).

2.1.6. Semantic fluency

The semantic categories are the same as the original study: Animals and jobs.

Within a minute each the participants will have to orally produce as many animals and jobs as possible (Witte et al., 2015). Thus, appraise word generation and semantic knowledge that are represented in temporal areas (Baldo, SChwartz, Wilkins, & Dronkers, 2006).

2.1.7 Sentence completion (broad context/less semantically induced)

The sentence structure and verb tenses were maintained, and it was necessary to change the Dutch proper names to Portuguese ones.

To evaluate speech production and reading, language dynamics and production of semantically and syntactically appropriate speech, the subjects must read aloud 25 sentences and complete them in a meaningful way (Witte et al., 2015). The clauses must be grammatically correct and despite this, the response consent a variety of responses. This task can be used in the supplementary motor area, the temporoparietal regions, the insula, the subcallosal fascicle and the ILF (Bello et al., 2007; Fontaine et al., 2002) (Fig.1F).

2.2. Ethical considerations

Prior to the start of the study, a request was made to the Ethics Committee of the Health Sciences Research Unit of Coimbra Nursing School, which was subsequently approved (Reference No. P545_01_19) as shown in Appendix I.

2.3. Participants

Data were collected between the months of May and August of 2019. Participants were recruited considering a non-probability sampling - snowball sampling (Fortin & Harel, 1999). The protocol was administered to one hundred and forty four (144) healthy adults volunteers, based on the inclusion criteria of the original study: 1) Portuguese as the native language; 2) no clinical antecedents of cardiovascular, neurological, psychiatric, language and/or speech development disorders; 3) no dependence on toxic substances (drugs or alcohol); 4) no hearing deficits; 5) no vision deficits; 6) no use of medication that can influence the protocol results; 7) Mini Mental State Examination (MMSE) results must be greater than/above 24/30, considering the cut-off for impairment – 23 (Crum, Anthony, Bassett, & Folstein, 1993; Witte et al., 2015). All participants were informed of the purpose of the study and signed informed consent forms (Appendix II). The number of participants per age group was defined considering the data from the original DuLIP. Average life expectancy is similar in both countries, Portugal 81,6 years of age and the Netherlands 81,8 years of age (PORDATA, 2017). Participants were from different parts of the country, with a variety of cultures and customs (North, Centre, Lisbon and Madeira island). Both female and male volunteers participated between the ages of 18 and 89 years.

2.4. Test administration

Before the protocol was administered, socio-demographic data were collected such as age, gender, years of education, laterality and district of the country where the participant lives (Appendix III).

In the original study, in order to exclude possible cognitive impairment, the MMSE was used, but this test is not validated for EP. Therefore, knowing that there is validation for EP of the Addenbrooke's Cognitive Examination III (ACE III) (Witte et al., 2015; Machado, Baeta, Pimentel, & Peixoto, 2015; Matías-Guiu et al., 2018), and it is possible to convert the ACE III results to MMSE final values, this was the test used in our study. It has been shown that the ACE III → MMSE score conversion has a high reliability with intra-class correlation coefficients (Matías-Guiu et al., 2018).

Three speech and language therapists administered independently the protocol but following specific rules, given by the original study. Thus, all tasks were performed in the same order. It was ensured that participants understood what was proposed to them. It was necessary to use a computer, so that participants could have access to a PowerPoint presentation whenever there were visual stimuli. There were pauses between the major tasks so that the participants could rest. It is important to remember that there are tasks to be performed during DES stimulation and, to do so, they must be accomplished within the 4 s time frame. Whenever time was up the slide would automatically pass and be accompanied by a beep called "laser sound". However, tasks such as judgment, fluency and semantic sentence completion (less semantically induced) had no time limit due to their complexity. If the participant correctly identified the target answer within the time frame, it would be given one point. All other answers given by participants were written verbatim. If self-corrections were made within the time frame they were considered right. One repetition was allowed for the auditory tests. All these criteria were defined by the three assessors (speech and language therapists), the answers were discussed among all, whenever there were doubts it would only be considered right or wrong after reaching a consensus.

2.5. Statistics

The data were analysed with IBM SPSS Statistics 24.

Given the participants' responses, it was possible to classify them as correct or incorrect. The percentage of the correct answers for each item was accounted for and all the items with values below 90% were excluded (Sbordone, 2000). This cut-point is used in neuropsychological batteries (Sbordone, 2000).

Data analysis was based on the original study and thus had to consider two age groups (18 to 54 years and more than 55 years), two gender groups (male and female) and two groups for years of education (more than 12 years and less than 12 years). Therefore, we considered the same age groups; male and female genders, and regarding the years of education 12 years were considered because in Portugal these are the compulsory school years (Livre, 2009).

To verify if the sample follows a normal distribution, the nonparametric Kolmogorov-Smirnov test was used (N>50) (Fortin & Harel, 1999). All semantic tasks did not follow the normal distribution, except the animal fluency and mean fluency of animals and jobs tests. As most tasks do not follow a normal distribution, nonparametric tests were used (Fortin & Harel, 1999).

In order to evaluate the effects of age, gender and years of education on each task, the nonparametric Mann-Whitney test was used. Initially a p-value of ≤ 0.05 was considered. Then the data was also analysed according to a p-value of ≤ 0.0024 – Sidak correction (Sidak, 1967). The latter p-value was utilized given that the original authors used it in their study and because multiple testing was involved (7 x 3 for age, gender and years of education) (Witte et al., 2015; Sidak, 1967). For each semantic test, data such as mean, median, ranges and cut-off scores will be presented considering the entire group but also between age/years of education combination. We considered the cut-offs as the original study, as they are the ones used in clinical practice, percentile 2 and 7 (Witte et al., 2015; Palmer, Boone, Lesser, & Wohl, 1998).

In order to verify if there is any relationship between cognitive impairments and the odd word out semantic task, the Spearman correlation test was used.

3. Results

The study has a sample of 144 participants: 62 participants are men and 82 are women; 121 are people aged between 18 and 54 years, and 23 are more than 55 years old with a mean of 36.81 years and with a range of 18 to 89; 32 have 12 years of education or less, and 112 have more than 12 years of education with a mean of 15.36, ranging from 4 to 24 years of education.

Thus, this Dissertation presents a higher percentage of: women, younger participants (18-54y), with more years of studies (>12y), from the central region and right-handed.

Table 1 shows the demographic data of the healthy 144 adults.

Table 1. - Demographic characteristics of the 144 participants.

Demographics	Mean	SD	Range
(A) Age, education, MMSE (mean, SD, range)			
Age in years	36.81	14.86	18-89
Education in years	15.36	4.14	4-24
MMSE	28.64	0.97	25-30
Demographics	Groups	Number of subjects	Percentage (%)
(B) Gender, age, education, district, handedness groups			
Gender	F	82	56.94
	M	62	43.06
Age	18-54y	121	84.03
	55+y	23	15.97
Education level	≤ 12y	32	22.22
	> 12y	112	77.78
Region	North	35	24.31
	Centre	94	65.28
	Lisbon	13	9.03
	Madeira	2	1.39
Handedness	L	3	2.08
	A	1	0.69
	R	140	97.22

(A) Legend: SD = standart deviation; MMSE = Mini Mental State Examination.

(B) Legend: F = female; M = male; y = years; L = left-handed; A = ambidexter; R = right-handed.

Considering the accuracy rate 90% of correct answers the semantic tasks that produced errors were: Reading with semantic odd word out; naming with semantic odd picture out; semantic association task and semantic sentence judgment. Of these, the task that produced the most errors were semantic association task, with 11 items eliminated, followed by reading with semantic odd word out with 5 items rejected, then semantic sentence judgment with 4 and finally naming with semantic pic out with 2 items removed. Many participants answered wrong or missed the response time limit of 4 s.

Bellow, an example of an item of each task with the highest error rates, will be presented:

- Semantic association task (61.11%): <*bola, boneco …*> (<ball, doll …>)

- Reading with semantic odd word out (83.33%): <*bola, boneco, lego, sabão*> (<ball, doll, lego, soap>)

- Semantic sentence judgment (85.42%): < *"O agricultor ordenha as vacas no celeiro."*> (<The farmer milks the cows in the stable>)

- Naming with semantic picture out (81,94%): <*gravata, vaca, luva*> (<tie, cow, glove>)

Considering the p-value ≤ 0.05 for 5 of the DuLIP-EP tasks (semantic association task; sentence completion-closed context; semantic sentence judgment; semantic fluency jobs; semantic mean fluency) there was a significant effect of gender, i.e., the female group got better results. Given the Sidak's ($p \leq 0.0024$) correction no significant effect was found in any task (Appendix IV).

For 5 DuLIP-EP tasks (reading with semantic odd word out; naming with semantic odd picture out; semantic fluency animals; semantic fluency jobs; semantic mean fluency) there was a significant effect of age: The lower the age (18-54y), the higher the scores, considering $p \leq 0.05$. Complying with the Sidak's (1967) correction value there were 5 tasks that are statistically significant (semantic odd word out, semantic odd pic out, semantic fluency animals, semantic fluency jobs and mean of fluency) (Appendix IV).

In all DuLIP-EP tasks there was a significant effect of years of education, except in sentence completion (open context). Therefore, results suggest that the higher the education level (>12), the higher the tasks scores, considering $p \leq 0.05$. Considering the Sidak's (1967) value, there were 5 tasks that were statistically significant (semantic odd word out, semantic odd pic out, semantic fluency animals, semantic fluency jobs and mean of semantic fluency) (Appendix IV).

Values such as mean, median, range and cut-off percentile 2 and 7, for the 144 participants as well as groups considering their age and years of education are shown in Appendix V. Group 1 includes young participants with lower education (n=19); in Group 2 we included young participants with higher education (n=102), group 3 contains 13 adults with more than 54 years old and lower education and finally group 4 is comprised of the older participants with higher education (n=10).

Considering the possibility of some relationship between cognitive ability and semantic intruder identification task, a moderate correlation ($r=0.410$) was observed between the MMSE result and the semantic task odd word out, which is statistically significant (sig=0.000), since $p \leq 0.05$ (Pestana & Gageiro, 2008), which also holds for the corrected Sidak's (1967) corrected value of $p \leq 0.0024$.

4. Discussion

During this study the semantic tasks of DuLIP were translated and adapted to the Portuguese population, and then applied to a group of normal participants in order to obtain normative data. This version of DuLIP considered the same aspects and characteristics as the original one. Therefore, it can also be used in pre, intra and post-operative surgeries with a patient with LGG, in awake brain surgery, making this protocol ground-breaking in Portugal.

All tasks and their items were discussed among three speech and language therapist and the original DuLIP authors and only after consensus did the items integrate the protocol. In order to be able to culturally adapt the 8 semantic tasks it was necessary to change some items considering the frequency of the word, copyright issues and it was necessary to change the proper names to Portuguese. Aspects such as word category, passive/active voice, time/verbal mode and sentence type and structure were maintained. Some images have also been altered, as they do not exist in the study by Ventura et. al (2014), however, whenever possible, images from the same semantic category were chosen.

The DuLIP-EP was administered to all participants and due to the minimum accuracy rate criteria of 90%, some items had to be removed and the total number of items for each task decreased, because participants did not respond within the 4 s time limit or answered incorrectly. So, the task reading with semantic odd word out has 20 items, 5 less than the original DuLIP; the naming with semantic odd picture out task has 23 items instead of 25 as in the original study; the semantic association task has 11 items less (14 original items were maintained); the semantic sentence completion, closed and broad context remained with the 25 items; the semantic sentence judgment task has 46 items, 4 less than the original.

Due to this, it will not be possible to make real comparisons with the results of the original study. However, it was possible to analyse the results obtained and consequently, it was observed that there was a significant effect of gender, because women had better results ($p \leq 0.05$). This ceases to be true when the Sidak (1967) correction is used, the same as in the original study (Witte et al., 2015). Regarding the effect of age, it was possible to observe that the lower the age, the higher the scores and the higher the education level, the higher the tasks scores, coinciding with the results of the original DuLIP (Witte et al., 2015). The test that caused the most errors was the semantic association task, and it was also the test where it was necessary to eliminate the largest number of items, which had also happened with the original DuLIP (Witte et al., 2015).

It was possible to divide the participants in 4 distinct groups, considering their age and years of education. The groups with better results in the semantic tests were group 2 and group 4, showing that the participants with more years of education have better outcomes.

Regarding the hypothesis raised on cognitive outcomes and their possible relationship with semantics, despite the correlation being statistically significant, it should be noted that this is a moderate correlation ($r=0.410$) and caution should be exercised when generalising the results.

This is corroborated by Deák (1973, p. 273) that has previously concluded that cognition and language (semantic) are co-dependent (Deák, 1973).

5. Conclusions

With this Dissertation it was possible to translate and adapt the semantic tasks of DuLIP to EP. The other areas (syntax, phonology, naming and articulation) were studied by Alves (2019) and Morgado (2019). This protocol will be used in neurosurgeries to remove LGG where the patient is awake and while DES is being performed, the patient will execute this language battery tests.

It was necessary to maintain the maximum of stimuli used in the original study, but it was sometimes not possible to keep this indication as cultural adaptation had to be considered. Still, characteristics such as word category, passive/active voice, time/verbal mode and sentence type and structure were maintained. Some words had to be exchanged considering their frequency and the proper names had to be changed. Some images were also modified because they were not included in the Portuguese validated study by Ventura et. al (2014).

In order to obtain normative data, following the inclusion criteria, 144 adults participated in the study. Some items had to be removed because of the accuracy rate (<90%); the tasks that revealed the highest error rates were reading with semantic odd word out; naming with semantic odd picture out; semantic association task and semantic sentence judgment.

Therefore, the semantic area has 8 tasks, including, the reading with semantic odd word (20 items), the naming with semantic odd picture out (23 items), the semantic association task (14 items), the semantic completion (closed and open context) has (25 items), the semantic sentence judgment (46 items) and the fluency task (animals and jobs) without a limited number of items.

Considering the statistical tests used and analysing the results it was possible to observe that the lower the age, the higher the scores and the higher the education level, the higher the tasks scores and that the women displayed better performances. Regarding a possible relationship between cognitive outcomes and the task of reading with semantic odd word out it was observed that there is a moderate correlation, relating semantics to cognitive ability.

This type of language assessments is of utmost importance for awake brain surgeries and consequently for patient well-being and quality of life.

5.1. Limitations and future work

The internal consistency, test-retest reliability, criterion validity and construct validity have yet to be analysed, but this was not the purpose of this Dissertation. In the future a study is suggested to validate DuLIP-EP and the number of items per task must be increased and these must be properly validated because it was not possible to compare the results obtained with the original study, due to the difference found in the number of items of each task.

The sample characteristics, which do not follow a normal distribution, prevented the use of more powerful tests (parametric tests). Therefore, it would be important, in the future, to increase the

number of participants. Another limitation is that, in the four groups, there are very different number of participants, so it would be important to ensure balanced groups in future work.

Most of the available studies were conducted with individuals during surgery, making the comparation with the normal population difficult to perform. It would be important to use the DuLIP-EP protocol with clinical cases, in order to understand its application and the patient's performance.

Researchers now have a version of DuLIP translated into EP, which could be easily adapted to clinical practice.

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Scientific Outputs Related to this M.Sc. Thesis

Publication

Jesus, L., J. Alves, M. Cardoso, and M. Morgado (2019). Linguistic Intraoperative Protocol. In Proceedings of the 10th International Conference of Experimental Linguistics (ExLing 2019), Lisbon, Portugal, pp. 121-124.

Oral Presentation

“Linguistic Intraoperative Protocol”. Oral presentation at the10th International Conference of Experimental Linguistics (ExLing 2019), Lisbon, Portugal, 25th of September 2019.

Grant Supporting the Participation in Conference

10th International Conference of Experimental Linguistics Grant from the Organisation Committee, to participate in the 10th International Conference of Experimental Linguistics (ExLing 2019), Lisbon, Portugal, 25th to 27th of September 2019.

APPENDIX I - Ethics approval

COMISSAO DE ETICA

da **Unidade Investigação em Ciências da Saúde: Enfermagem** (UICISA: E)

da **Escola Superior de Enfermagem de Coimbra** (ESEnfC)

Parecer Nº 545/ 01-2019

Título do Projecto: Tradução, Adaptação e Validação para Portugal do Dutch Linguistic Intraoperative Brain Protocol (DuLIP)

Identificação das Proponentes

Nome(s): Joana Patrícia Gomes Alves, Mafalda Inês Martins Cardoso e Mariana Morgado Oliveira Martins

Filiação Institucional: Escola Superior de Saúde da Universidade de Aveiro (alunas de mestrado em terapia da fala)

Investigador Responsável/Orientador: Prof. Luís Miguel Teixeira de Jesus

Relator: Sofia Raquel Teixeira Nunes

Parecer

Considerando a avaliação das competências linguísticas pré, intra e pós-operatórias em doentes com lesões tumorais a nível cerebral e submetidos a estimulação elétrica cerebral, este estudo tem como objetivo traduzir e adaptar ao português europeu o instrumento DuLIP e validar o referido à população portuguesa normal. Segundo os investigadores, será um estudo do tipo metodológico com fase qualitativa e quantitativa (a primeira respeita a tradução e adaptação do instrumento e a segunda respeita à aplicação do mesmo).

A data de início de colheita de dados encontra-se prevista para 1 de fevereiro de 2019 e o término a 1 de março de 2022, pelo que à data atual terão os investigadores de adaptar as mesmas.

A amostra agregará no mínimo 140 pessoas da população portuguesa, com critérios de inclusão bem definidos. Será realizada uma amostragem por conveniência em diversas regiões de Portugal.

Os investigadores irão utilizar para além dos instrumentos de colheita de dados, instrumentos que permitam aferir da compatibilidade com os critérios de inclusão dos participantes.

Referiram os investigadores que toda a informação recolhida será tratada de forma confidencial, onde são garantidas a voluntariedade e a autonomia dos participantes. Os dados serão utilizados mas os nomes dos participantes serão substituídos por códigos e só os investigadores terão acesso aos dados. Contudo, é referido que irão recolher o nome dos participantes mas que estarão em destacáveis que serão retirados. Foram verificadas algumas situações na identificação dos utentes e no folha informativa que prontamente foram corrigidas pelos investigadores.

Sendo assim, somos do parecer que o projeto pode ser aprovado sem restrições de natureza ética.

O relator:

Data: 12/03/2019 O Presidente da Comissão de Ética: ______________

Unidade de Investigação em Ciências da Saúde

Escola Superior de Enfermagem de Coimbra

FCT Fundação para a Ciência e a Tecnologia

APPENDIX II- Participants' informed consent

Consentimento Informado, Livre e Esclarecido para Participação em Investigação de acordo com a Declaração de Helsínquia

(Helsínquia 1964; Tóquio 1975; Veneza 1983; Hong Kong 1989; Somerset West 1996; Edimburgo 2000; Washington 2002; Tóquio 2004; Seoul 2008)

Título do estudo: Tradução, Adaptação e Validação para Portugal do *Dutch Linguistic Intraoperative Brain Protocol (DuLIP).*

Enquadramento: Este estudo enquadra-se no Mestrado em Terapia da Fala, da Escola Superior de Saúde da Universidade de Aveiro orientado pelo Professor Doutor Luís Jesus e visa traduzir e adaptar um instrumento de avaliação da linguagem em contexto cirúrgico e pós-cirúrgico, mais especificamente das áreas semântica, fonológica e morfossintática. Avalia ainda a articulação verbal. A sua colaboração contribuirá para a adaptação de um teste inovador para o português europeu e, posteriormente, para a melhor compreensão do mapeamento cerebral no que concerne às áreas da linguagem e fala.

Explicação do estudo: Este é um estudo científico que envolve entrevistas e aplicação de testes em local e horário que lhe sejam convenientes. Será solicitada a resposta a determinadas questões demográficas e clínicas. Além disso, será pedida a resposta a determinados itens específicos que o teste a validar contempla.

O Dutch Linguistic Intraoperative Protocol (DuLIL) é um instrumento de origem Holandesa, criado e validado para a avaliação de competências de linguagem em contexto pré, intra e pós cirúrgico em pacientes diagnosticados com lesões tumorais a nível cerebral e submetidos a estimulação elétrica direta (DES) – uma técnica utilizada em neurocirurgia com o paciente acordado, que permite o mapeamento das regiões cerebrais corticais e subcorticais. Embora esta técnica seja cada vez mais utilizada e já considerada um procedimento *gold standard* em neurocirurgia, ainda carece de instrumentos validados para a avaliação das competências a testar no aparato cirúrgico.

No que refere às lesões tumorais que afetam as áreas da linguagem, sabe-se que existem benefícios na utilização desta técnica relativamente ao *outcome* linguístico pós-operatório. Não obstante, a existência de métodos de identificação das áreas associadas a estas competências, validados para os contextos anteriormente referidos são escassos e, no caso do Português Europeu, de acordo com a pesquisa bibliográfica realizada, inexistentes. Assim, este estudo poderá contribuir para a prática clínica das áreas de Neurocirurgia, Neurologia, Terapia da Fala, Neurolinguística e Neuropsicologia, maximizando os resultados e possível potencial de reabilitação dos utentes. Permitirá ainda contribuir para o melhor mapeamento de regiões e trajetórias cerebrais, corticais e subcorticais, relacionadas com a linguagem, nomeadamente nas áreas da fonologia, semântica e sintaxe. As capacidades articulatórias também são contempladas no instrumento.

Condições de financiamento: A participação no estudo não é remunerada. A decisão de participar no mesmo é inteiramente sua. Caso aceite participar, poderá desistir a qualquer momento, bem como recusar qualquer procedimento, sem ser penalizado por isso.

Possíveis riscos ou desconforto: As tarefas não apresentam quaisquer riscos ou desconforto para os participantes.

<u>Confidencialidade e anonimato:</u> A confidencialidade dos dados e dos envolvidos no estudo está salvaguardada. A identificação pessoal ou dados alusivos à mesma não serão disponibilizados a outro grupo ou instituição.

Gratas pela disponibilidade demonstrada, encontramo-nos disponíveis para esclarecer qualquer questão relativa ao estudo.

Contacto para possível esclarecimento de dúvidas:

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Este documento é composto de 2 páginas e feito em duplicado: uma via para o/a investigador/a e outra para a pessoa que consente

DECLARAÇÃO DE CONSENTIMENTO

de acordo com a Declaração de Helsínquia

(Helsínquia 1964; Tóquio 1975; Veneza 1983; Hong Kong 1989; Somerset West 1996; Edimburgo 2000; Washington 2002; Tóquio 2004; Seoul 2008)

Título do estudo: Tradução, Adaptação e Validação para Portugal do *Dutch Linguistic Intraoperative Brain Protocol* (DuLIP).

Eu, ____, abaixo-assinado, declaro ter lido e compreendido este documento, bem como as informações orais que me foram fornecidas pela(s) pessoa(s) que assinaram abaixo.

Foi-me dada a oportunidade de fazer as perguntas que julguei necessárias, e a todas obtive resposta satisfatória.

Tomei conhecimento de que, de acordo com as recomendações da Declaração de Helsínquia, a informação ou explicação que me foi prestada versou os objetivos, os métodos, os benefícios previstos, os riscos potenciais e o eventual desconforto. Além disso, foi-me garantida a possibilidade de, a qualquer momento, recusar participar no estudo sem qualquer tipo de comprometimento.

Eu compreendo que os resultados do estudo podem ser publicados em revistas científicas, apresentados em conferências e usados noutras investigações, sem que haja qualquer quebra de confidencialidade. Portanto, dou autorização para a utilização dos dados para esses fins. Assim, aceito participar neste estudo e permito que a utilização dos dados que de forma voluntária forneço, confiando que são utilizados confinadamente para o que me foi descrito e me é garantida, pelos investigadores, a confidencialidade e anonimato dos mesmos.

P'los investigadores, O participante,

____________________________________ ____________________________________

_________, ___ de __________________ de 2019

Este documento é composto de 2 páginas e feito em duplicado: uma via para o/a investigador/a e outra para a pessoa que consente

Appendix III – Personal information document

CÓDIGO___________

PROTOCOLO PARA RECOLHA DE DADOS

Data da realização do teste: ___/___/_____

Dados recolhidos por: ________________

IDENTIFICAÇÃO PESSOAL

Região de residência: ____

Sexo: Masculino (__) Feminino (__)

Data de nascimento: ___/___/_____ Idade ____ anos

FORMULÁRIO DE INFORMAÇÃO PESSOAL

Lateralidade: Destro (__) Esquerdino (__)

Grau de escolaridade: Não sabe ler nem escrever (__) Sabe ler e escrever (__)

Ensino primário (__) 2º ciclo (__) 3º ciclo (__) Ensino secundário (__)

Pós-graduação (__) Licenciatura (__) Mestrado (__) Doutoramento (__)

Indicar o número de anos de estudos: ____

Situação de empregabilidade atual: Estudante (__) Empregado (__) Desempregado (__) Reformado (__)
Profissão ou antiga profissão: ____

Informação linguística

Língua materna: Português (__) Outro (__)

Qual a língua que fala em casa? Português (__) Outro (__) Especifique: ___________________________

Qual a língua na qual recebeu educação? Português (__) Outro (__) Especifique: ___________________

É fluente noutras línguas? Português (__) Inglês (__) Francês (__) Espanhol (__) Especifique: __________

História clínica

Antecedentes neurológicos (e.g. epilepsia)? Sim (__) Não (__) Especifique: ________________________

Antecedentes psiquiátricos? Sim (__) Não (__) Especifique: ____________________________________

Alterações de aprendizagem ou comportamentais? Sim (__) Não (__) Especifique: __________________

Alterações de fala e/ou linguagem? Sim (__) Não (__) Especifique: ______________________________

Alterações relacionadas com visão/perceção de cores? Sim (__) Não (__) Corrigida (___)

Especifique: ____

Alterações relacionadas com audição? Sim (__) Não (__) Corrigida (__) Especifique: _________________

Dependente de substâncias tóxicas álcool ou drogas? Sim (__) Não (__) Especifique: ________________

Medicação que possa influenciar os resultados (e.g. medicação indutora de sono; psicofármacos; medicação neuroléptica)? Sim (__) Não (__) Especifique: ______________________________________

Antecedentes cardiovasculares: Sim (__) Não (__)

Observações (e.g. observação comportamental durante o teste):

____

____

____

Appendix IV – P-values per test

DuLIP-EP test (maximum score)	Age group	Education groups	Gender groups
Reading with semantic odd word out (n = 20); MWU	U = 691,000; Z = -4,400; p < ,000	U = 951,500; Z = -4,653; p < ,000	U = 2378,500; Z = -,760; p = ,447
Naming with semantic odd picture out (n = 23); MWU	U = 995,500; Z = -3,049; p < ,002	U = 1308,500; Z = -3,281; p < ,001	U = 2464,000; Z = -,444; p = ,657
Semantic association (n = 14); MWU	U = 1153,500; Z = -1,522; p < ,128	U = 1390,000; Z = -2,265; p < ,024	U = 2042,500; Z = -2,363; p = ,018
Semantic sentence completion (closed context) (n = 25); MWU	U = 1122,000; Z = -1,837; p < ,066	U = 1372,500; Z = -2,520; p = ,012	U = 2073,500; Z = -2,363; p = ,018
Semantic fluency animals (no maximum score); MWU	U =753,500; Z = -3,485; p < ,000	U = 1029,500; Z = -3,671; p < ,000	U = 2116,000; Z = -1,722; p = ,085
Semantic fluency jobs (no maximum score); MWU	U = 665,500; Z = -3,966; p < ,000	U = 927,000; Z = -4,164; p < ,000	U = 1804,500; Z = -2,981; p = ,003
Semantic fluency means (no maximum score); MWU	U = 628,500; Z = -4,164; p < ,000	U = 849,500; Z = -4,533; p < ,000	U = 1916,500; Z = -2,526; p < ,012
Semantic sentence completion (broad context) (n = 25); MWU	U = 1298,000; Z = -1,108; p < ,268	U = 1605,000; Z = -1,953; p < ,051	U = 2454,000; Z = -,772; p = ,440
Semantic sentence judgment (n = 46); MWU	U = 1128,500; Z = -1,655; p < ,098	U = 1411,500; Z = -2,110; p < ,035	U = 1909,000; Z = -2,947; p = ,003

Legend: p = p-value; MWU = Mann-Whitney U test; ➔ p <,05; ➔ p <,0024 (Sidak correction)

Appendix V - Descriptive statistics for the semantic DuLIP-EP tests

Semantic Test (maximum score)	Parameters	Group 1 Age 18-54y Edu ≤12y n = 19	Group 2 Age 18-54 y Edu >12y n = 102	Group 3 Age > 54y Edu ≤12y n = 13	Group 4 Age > 54y Edu >12y n = 10	Total Age ≥ 18y Edu ≥ 6 y n = 144
Reading with semantic odd word out (n = 20)	Mean	18,79	19,55	14,85	19,50	19,02
	Median	20,00	20,00	16	19,50	20,00
	Range	12-20	14-20	5-20	19-20	5-20
	Cut-off Pc 2	--	15,12	--	--	11,80
	Cut-off Pc 7	--	18,00	--	--	16,00
Naming with semantic odd picture out (n = 23)	Mean	22,74	22,74	21,38	19,50	22,63
	Median	23,00	23,00	22,00	19,50	23,00
	Range	21-23	18-23	18-23	19-20	18-23
	Cut-off Pc 2	--	20,00	--	--	18,90
	Cut-off Pc 7	--	22,00	--	--	21,00
Semantic association (n = 14)	Mean	13,32	13,54	12,23	13,60	13,40
	Median	14,00	14,00	13	14,00	14,00
	Range	12-14	11-14	7-14	12-14	7-14
	Cut-off Pc 2	--	11,00	--	--	10,70
	Cut-off Pc 7	--	12,00	--	--	12,00
Semantic sentence completion (closed context) (n = 25)	Mean	24,37	24,61	23,69	24,80	24,51
	Median	25,00	25,00	24,00	25	25,00
	Range	22-25	19-25	21-25	24-25	19-25
	Cut-off Pc 2	--	22,06	--	--	21,90
	Cut-off Pc 7	--	23,00	--	--	23,00
Semantic fluency animals (no maximum score)	Mean	21,74	24,00	16,77	21,50	22,88
	Median	20,00	24,00	17,00	20,50	23,00
	Range	17-34	11-37	8-25	15-29	8-37
	Cut-off Pc 2	--	13,00	--	--	10,70
	Cut-off Pc 7	--	17,00	--	--	15,15
Semantic fluency jobs (no	Mean	17,74	20,04	13,00	18,10	18,97
	Median	17,00	20,00	12,00	18,00	19,00
	Range	10-28	10-32	11-16	12-23	10-32

maximum score)	Cut-off Pc 2	--	11,06	--	--	10,90
	Cut-off Pc 7	--	13,00	--	--	12,00
Semantic fluency means (Animals and Jobs – no maximum score)	Mean	19,66	22,03	14,88	19,80	20,92
	Median	19,00	22,00	14,00	20,00	21,00
	Range	14,50-29,50	11,50-32,50	9,50-20,50	14,50-25,50	9,50-32,50
	Cut-off Pc 2	--	11,59	--	--	11,50
	Cut-off Pc 7	--	15,61	--	--	14,08
Semantic sentence completion (broad context) (n = 25)	Mean	24,89	24,94	24,69	25,00	24,92
	Median	25,00	25,00	25,00	25,00	25,00
	Range	24-25	24-25	23-25	25-25	23-25
	Cut-off Pc 2	--	24,00	--	--	24,00
	Cut-off Pc 7	--	25,00	--	--	24,00
Semantic sentence judgment (n = 46)	Mean	45,42	45,56	44,23	45,60	45,42
	Median	46,00	46,00	45,00	46,00	46,00
	Range	44-46	43-46	38-46	44-46	38-46
	Cut-off Pc 2	--	44,00	--	--	42,90
	Cut-off Pc 7	--	44,21	--	--	44,00

Legend: n = numbers; Pc = percentile, y = years, edu = years of education.

* The percentiles 2 and 7 of the groups with higher N were taken into consideration, because only those have significant differences in the values.