

Neuroimaging investigation of executive functions: evidence from fNIRS

Yves Joannette

Ana Inés Ansaldo

*Faculté de Médecine, Université de Montréal
Montreal, Canada*

Maria Alice de Mattos Pimenta Parente

*Universidade Federal do Rio Grande do Sul – UFRGS
Porto Alegre, RS, Brasil*

Rochele Paz Fonseca

Christian Haag Kristensen

*Pontifícia Universidade Católica do Rio Grande do Sul – PUCRS
Porto Alegre, RS, Brasil*

Lilian Cristine Scherer

*Universidade de Santa Cruz do Sul – UNISC
Santa Cruz do Sul, RS, Brasil*

ABSTRACT

Functional Near-Infrared Spectroscopy (fNIRS) has emerged as a valuable tool to investigate human cognition. One of the most relevant cognitive aspects to be further explored is the role of executive functions (EF) in cognitive tasks' performance. The aim of this article is to review empirical studies on EF processing conducted by means of fNIRS. This systematic review has shown, among other findings, that the majority of the studies has focused (a) on the neural correlates of cognitive processing, (b) on the EF components of verbal fluency and Stroop tasks, (c) mainly on healthy young adults populations, and (d) on clinical samples, represented most frequently by schizophrenic patients. The reviewed technique can be considered valid for examining neurobiological correlates of executive functions.

Keywords: Executive functions; neuroimaging; fNIRS; systematic review.

RESUMO

Estudos de neuroimagem sobre funções executivas: evidências da técnica fNIRS

A Espectroscopia de Infravermelho Próximo Funcional (fNIRS) tem se mostrado uma ferramenta importante na investigação da cognição humana. Dentre os processos psicológicos que necessitam ser detalhadamente investigados destacam-se as funções executivas (FE). O presente artigo buscou revisar estudos empíricos das FE realizados com fNIRS. Esta revisão sistemática mostrou, dentre outros achados, que a maioria das pesquisas focalizou: (a) os correlatos neurais do processamento cognitivo, (b) os componentes executivos de tarefas de fluência verbal e Stroop, (c) amostras com predominância de participantes adultos jovens saudáveis, e (d) populações clínicas frequentemente representadas por adultos esquizofrênicos. A técnica revisada pode ser considerada válida para examinar correlatos neurobiológicos das FE.

Palavras-chave: funções executivas; neuroimagem; fNIRS; revisão sistemática.

RESUMEN

Estudios de neuroimagen sobre funciones ejecutivas: evidencias de fNIRS

La espectrografía funcional Infra-rojo (fNIRS) surge como una herramienta valiosa en la investigación de la cognición humana. Uno de los aspectos cognitivos más relevantes que merece ser explorado en profundidad es el rol de las funciones ejecutivas (FE). El objetivo principal de este artículo es la revisión de estudios empíricos sobre FE con fNIRS. El resultado de ésta revisión sistemática muestra que la mayoría de los estudios realizados aborda (a) el correlato neuronal de procesamiento cognitivo, (b) los componentes ejecutivos implicados en la fluencia verbal y en el efecto Stroop, (c) principalmente en adultos jóvenes saludables y (d) las poblaciones clínicas representadas en su mayoría por pacientes esquizofrênicos. La técnica reseñada puede ser considerada válida para examinar los análogos neurobiológicos de las funciones ejecutivas.

Palabras claves: funciones ejecutivas; neuroimagen; fNIRS; revisión sistemática.

INTRODUCTION

This article aims to review the literature regarding the study of executive functions (EF) conducted with functional Near-Infrared Spectroscopy (fNIRS). This promising neuroimaging technique was initially applied to study cortical activity by Jobsis (1977), who first demonstrated the efficiency of the penetration of near-infrared lights in the skull to monitor cortical activation. A decade after the seminal work of Jobsis, a large amount of studies of brain functioning using fNIRS has emerged.

This neuroimaging technique consists of irradiating near-infrared light, carried by an optical fiber, to the scalp. The light emitted by the source propagates through skin, skull, and brain, and is captured by detectors, following a curve on the superficial structure of the brain (cortex and sub-cortical white matter up to 1 cm deep). Cognitive tasks performance activates specific cortical brain areas, which require an increase in blood supply. Hemoglobin (Hb) present in the blood partially absorbs this light; therefore, the residual light unabsorbed by tissue can be captured by the detector. The blood oxygenation level dependent (BOLD) effect is the basic principle underlying functional Magnetic Resonance Imaging (fMRI) and fNIRs. However, only fNIRS can measure changes in both oxygenated (HbO) and deoxygenated (HbR) hemoglobin. As fNIRS sources and detectors are located on the scalp, the technique provides less spatial resolution than fMRI. Thus, a certain number of studies has followed the 10x20 measurement system proposed by Jasper (1958), used in Electroencephalographic (EEG) and Event-Related Potentials (ERP) studies (Hock et al., 1997; Kono et al., 2007; Quaresima, Ferrari, Sluijs, Menssen and Colier, 2002; Villringer and Chance, 1997).

In this context, the fNIRS technique has emerged as an alternative tool, due to (a) practical reasons – portability favors its use in hospitals as well as in clinical settings; (b) cost-effectiveness – the equipment is far less expensive than fMRI, for example; (c) relative tolerance to movements – it is not as sensitive to movement as fMRI scanners; it can even be used simultaneously to physical activities; (d) high temporal resolution – in the order of milliseconds, as compared to seconds with fMRI; and (e) ecological validity for task presentation and response (participants can perform the tasks in a comfortable position, with no noise being generated by the equipment). Moreover, it is suitable for the presentation of more complex tasks, such as discourse comprehension assessment. The inclusion of stimuli longer than words or sentences imposes difficulties for their presentation in

the majority of the other neuroimaging techniques. In addition, fNIRS is a non-invasive neuroimaging tool, since there is no need to inject radioactive contrast, and the wavelengths of the light used are not harmful. Therefore, data acquisition can be repeated, representing an advantage in both clinical and research settings where patients need to be followed-up or subjects are participating in research with a repeated measures design. Considering clinical populations and children, fNIRS represents a valuable tool, since participants are not exposed to the constrained fMRI environment. Moreover, there are no contraindications to its use, since participants can undergo the experiment using devices such as pace-markers, arterial clips and implants, as well as wearing their own glasses and hearing aid devices. Finally, it represents a particularly valuable tool for investigations in which time of activation is crucial, as it registers activations in the order of milliseconds, compared to seconds in fMRI acquisitions (Khoa and Nakagawa, 2007; Kono et al., 2007; Villringer and Chance, 1997).

The fNIRS technique also has its limitations. Its most important disadvantage is its lower spatial resolution as compared to fMRI. This related to the depth reached by the lights (although under constant refinement, its measures are nowadays still restricted to the brain surface, what does not allow its application to certain studies) and the quality of the signs captured, due to some light scattering produced by brain tissues (Koizumi et al., 2003; Quaresima et al., 2005). However, the lack of specific anatomical point of reference can be minimized by its association to the use of the 10x20 system and/or to frameless stereotaxic device using an anatomical MRI for guiding optodes placement.

Despite the existence of these limitations, fNIRS has already proved to be a reliable technology for the study of cognitive processing. As stated by Strangman, Boas and Sutton (2002), “for investigation of cortical activation [...] and especially when referenced to an external landmark system (e.g. the international 10/20 system), diffuse optical methods can provide opportunities unavailable with any other existing technology” (p. 690).

Among different cognitive processes, the investigation of EF has a far-reaching tradition in the neuropsychological literature (e.g., Luria, 1966, 1973). Within this view, EF are necessary for programming, controlling, and verifying behavioral activity and human mentation. EF have been broadly referred to as “higher-level” cognitive functions, which are implicated in the control and the regulation of “lower-level” processes (Alvarez and Emory, 2006). Although there is substantial variation regarding the

definition of the EF construct, some of its component processes generally cited in the neuropsychological literature under the EF label are: planning, initiation, sequencing, inhibition, cognitive flexibility, categorization and monitoring complex goal-directed behavior (Ardilla, *in press*; Fuster, 1997, 2000; Goldberg, 2001; Grafman, 1999; Roberts, Robbins and Weiskrantz, 1998; Royall et al., 2002; Smith and Jonides, 1999; Stuss and Alexander, 2000). In Lezak, Howieson and Loring's (2004) view, EF "consist of those capacities that enable a person to engage successfully in independent, purposive, self-serving behavior" (p. 35).

The cognitive processes subsumed under the EF construct have been historically linked with the frontal lobes (Alvarez and Emory, 2006; Pennington, 1997). The origins of this linkage can be traced back to the late 19th and early 20th centuries, when behavioral alterations were clinically assessed in cases of frontal pathology, including changes in personality, emotion regulation, and motivation (Ardilla, *in press*; Royall et al., 2002). Over the last decades, due to developments in functional neuroimaging and molecular biology, as well as advances in theoretical models, a far-more complex picture of brain-behavior interactions emerged (Brocki, Fan and Fossella, 2008; Chan, Shum, Touloupoulou and Chen, 2008; Diamond, Briand, Fossella and Gehlbach, 2004; Fassbender et al., 2004; Ravizza and Carter, 2008). Briefly, the neural substratum of the EF can be conceptualized not only in terms of frontal areas, but as distinct frontal-subcortical networks – including dorsolateral prefrontal, lateral orbitofrontal, and anterior cingulate circuits (Collette and Van der Linden, 2002; Melrose, Poulin and Stern, 2007; Robbins, 2007; Royall et al., 2002; Sbordone, 2000; Tekin and Cummings, 2002), as well as posterior regions of the brain (Collette, Hogge, Salmon and Van der Linden, 2006). Within this view, as stated by Alvarez and Emory (2006), while concluding their meta-analysis on this subject, the participation of the frontal lobes in EF is a necessary, but insufficient requirement.

When it comes to neuroimaging research on EF processing, there are much more studies applying fMRI as compared to any other available neuroimaging tool (Davidson, Amso, Anderson and Diamond, 2006; Monchi, Ko and Strafella, 2006; Sylvester et al., 2003). On the other hand, as stated before, fNIRS has some critical features that are particularly suitable to the investigation of EF, including temporal resolution and ecological validity for task presentation and response. To our knowledge, the emerging literature on the fNIRS investigation of EF has not been reviewed yet. Understanding how the brain instantiates cognitive processes required to perform executive

tasks in a dynamic manner is still a challenge (Fassbender et al., 2004). Therefore, the goal of this study was to undertake a systematic review of the potential of fNIRS to investigate EF in humans.

METHOD

The systematic review of the literature was conducted from February to July, 2008, in the following databases: International Pharmaceutical Abstracts (SilverPlatter), Nursing Journals (ProQuest), PsycINFO (SilverPlatter), PubMed/Medline (NLM), SciELO Brasil, SPORT Discus (EBSCO), and Web of Science (ISI). Keywords used were "executive function" and "NIRS", and publication date was set to include references ranging from 1997 to 2008. From the 15 papers originally retrieved by this search, 13 were kept in this review. Two papers were not included because they did not clearly mention the EF component under investigation. Instead, the components were tangentially approached, since the main aims of the articles were to examine cortical oxygenation changes during lexical decision on words and pseudowords, a language component (Hofmann et al., 2008), and to establish the measurement of functional brain activity during alertness – which is a basic function within attention (Hermann, Woidich, Schreppel, and Fallgatter, 2008). The 13 articles were then analyzed with a focus on Objective, Method and Results sections. The selection criteria for including articles were the following: 1) being an empirical study; 2) exclusively utilizing fNIRS as a neuroimaging tool; 3) assessing at least one executive component clearly specified, and 4) adopting a neuropsychological task which is clearly associated to EF processing.

RESULTS

The goal, methodology and main results of the 13 empirical studies reviewed are summarized in Table 1.

Concerning the aims of the studies reported on the table, 46.15% of the total amount are characterized by their interest in identifying a pattern of cortical activation (mainly in prefrontal regions) elicited by cognitive performance (studies 1, 3, 4, 5, 6 and 11), 30.77% showed interest in the comparison of the patterns of activation among clinical and control groups (studies 2, 8, 12 and 13), and the remaining 23.07%, on developmental changes of activation (studies 7, 9 and 10). Regarding the assessed EF components, 23.07% of the investigations focused on verbal fluency (2, 6 and 8), other 23.07% on Stroop

TABLE 1
Features of fNIRS studies on executive functions

<i>Studies</i>	<i>Aim(s)</i>	<i>Executive components</i>	<i>Participants</i>	<i>Instruments</i>	<i>Results</i>
(1) Boecker et al. (2007)	To investigate rCBF in R and L PFC during the performance of a stop-change paradigm	I	16 healthy adults (age 23.5)	Stop-signal task modified (stop-change)	– activation of L and R PFC, with rCBF L < R
(2) Ehlis et al. (2007)	To investigate rCBF during performance in verbal fluency tasks by schizophrenic	CG, wM(v)	12 schizophrenic patients (age 34.2, educ. 10.9) and 12 matched CTR (age 33.6, educ. 11.8)	Verbal fluency: phonological and semantic	– significant frontal HbO increase in healthy controls, L > R; – functional deficits in frontal HbO activation in schizophrenics
(3) Ehlis et al. (2005)	To investigate rCBF during performance on the Stroop task	I, wM(v)	10 healthy adults (age 26.9)	Stroop task	– significant L frontal (inferior) HbO (and total Hb) increase during interference task
(4) Fallgatter and Strik (1998)	To investigate frontal rCBF during performance on WCST	CG, P, I	10 healthy adults (age 30.0)	WCST	– significant L and R frontal HbO increase, no hemispheric differences
(5) Herrmann et al. (2005)	To investigate frontal rCBF during response inhibition	I	9 healthy adults (age 22.9)	Go/No-Go	– significant L and R frontal (inferior) HbO increase and HbR decrease during inhibition phase
(6) Jayacar et al. (2005)	To investigate frontal rCBF during performance in verbal fluency tasks	CG, wM(v)	17 healthy adults (age 32.0)	Verbal fluency: phonological (C, F, L) and semantic (animals)	– significant L and R frontal HbO increase during word generation; – no differences related to handedness
(7) Kwee and Nakada (2003)	To investigate age-related alterations in DLPFC rCBF	wM(v), P	60 healthy adults (age-range: 20 to 90)	WAIS-III subtests: picture completion, matrix reasoning, picture arrangement	– significant age-related decrease in DLPFC activation
(8) Schecklmann et al. (2007)	To investigate rCBF during performance in verbal fluency tasks associated with alcohol dependency	CG, wM(v)	12 alcohol dependent patients (age 43.9) and 12 matched healthy CTR	Verbal fluency: phonological and semantic	– decrease in activation (lower HbO) and the localization more restricted to inferior frontal areas in alcohol dependent patients
(9) Schoroeter, Zysset, Kruggel, et al. (2003)	To investigate frontal rCBF during performance in Stroop task across development	I, wM(v)	14 healthy young adults (age 23.9) and 14 healthy elderly adults (age 65.1)	Stroop task (modified)	– significant PFC (lateral) activation related to interference (young and elderly); – age-related decrease in rCBF PFC (lateral) during functional activation
(10) Schoroeter, Zysset, Wahl, et al. (2003)	To investigate frontal rCBF during performance in Stroop task across development	I, wM(v)	23 healthy children (age 10.4, educ. 2-8) and 14 young adults (age 23.9, educ. 10-15)	Stroop task (modified)	– significant L PFC (lateral) HbO increase and HbR decrease in children during interference; – rCBF (related to interference) increased with age in DLPFC (correlated with increase in performance)
(11) Shibuya-Tayoshi et al. (2007)	To investigate frontal rCBF during performance in a set-shifting task	I, wM(s)	41 healthy adults (age 22-49)	TMT	– greater PFC increase of HbO during TMT Part B than during Part A
(12) Watanabe and Kato (2004)	To investigate L frontal rCBF during performance in verbal fluency and span tasks by schizophrenics	CG, wM(v)	62 schizophrenia patients (age 40.1, educ. 12.9) and 31 healthy adults (age 36.1, educ. 13.6)	Verbal fluency (phonological); letter-number span	– smaller increase in frontal HbO in schizophrenic patients
(13) Weber et al. (2005)	To evaluate prefrontal rCBF during performance in a set-shifting task in ADHD	I, wM(s)	11 ADHD boys (age 10.4) and 9 healthy CTR (age 11.3)	TMT (modified)	– increase L PFC oxygenation in controls; – imbalance between HbO and HbR in ADHD

NOTES: L = left; R = right; PFC = prefrontal cortex; DL = dorsolateral; rCBF = regional cerebral blood flow; HbO = oxygenated hemoglobin; HbR = deoxygenated hemoglobin; CTR = controls; Age is presented in terms of mean values; educ = number of years of formal education; WCST = Wisconsin Card Sorting Test; TMT = Trail Making Test (Parts A&B); ADHD = Attention Deficit Hyperactivity Disorder; Dimensions of executive functions (EF) refer to those developed in factor-analytic studies, including Concept Generation (CG), Inhibition (I), spatial (s) and verbal (v) Working Memory (wM), and Planning (P) (see Royal et al., 2002).

interference (3, 9 and 10), 15.38% on inhibition (1 and 5), 15.38 on executive central of working memory (7 and 12), while 7.69% analyzed cognitive flexibility (11). In addition, one study – 7.69% (11) – used the Wisconsin Card Sorting Test for eliciting EF processing.

Regarding the sample examined in the investigations, healthy participants were the majority – 69.2% (studies 1, 3, 4, 5, 6, 7, 9, 10 and 11). Concerning age, young adults were the main population, present in all of the studies, followed by middle-aged adults, present in 15.38% of the studies (8 and 11), and by elderly adults, also represented in 15.38% of the investigations (7 and 9). The least investigated populations were children (10) and oldest-old adults (7) (7.69% – two studies sampling each one of these groups). Considering education level of the participants, only two healthy samples had their education categorized, both with high education levels (10 and 12). The other 30.8% of the studies included clinical samples, compared to matched controls. From clinical studies, 15.38% investigated schizophrenic patients (2 and 12), 7.69%, alcohol dependent individuals (8), and 7.69%, patients with attention-deficit hyperactivity disorder (13).

Besides sample features, the papers were also characterized considering the neuropsychological task(s) adopted to assess EF processing. The most frequently used instruments were the following, presented in descendent order: verbal fluency (30.77% of the investigations, with the phonemic criterion used in four studies – 2, 6, 8 and 12 – and the semantic one, in three – 2, 6 and 8), Stroop task (23.07% – 3, 9 and 10), Trail Making Test – TMT (15.38% – 11 and 13), followed by stop-change task (1), letter number span test (12), go-no go tasks (5), application of the Wisconsin Card Sorting Test – WCST (4) and of some subtests from WAIS-III (7) (7.69% each).

Finally, considering the aims posed by each study and their findings, 12 out of 13 analyzed the cerebral blood flow changes generated by the selected tasks in the frontal cortex, bilaterally (92.3%), while one of them (2) investigated temporal-frontal correlations (7.69%). One of the studies (3), along with a bilateral frontal activation analysis, had a special concern in verifying the patterns of blood changes specifically in the left inferior frontal brain area. The findings brought by the studies are the following: studies 1 and 5, which analyzed response inhibition, found strong left and right hemisphere activation in frontal lobes (study 1 reported a higher right hemisphere activation as compared to the one registered in the left hemisphere). Studies 2 and 12, which investigated cerebral blood flow changes in schizophrenic

participants' performance, reported reduced frontal regions activation while schizophrenic participants solved the tasks as compared to healthy participants' activation patterns. Investigation number 3, which analyzed Stroop interference, reported higher activation in the left hemisphere inferior frontal areas. Studies 4 and 6 (using the WCST and the verbal fluency task, respectively), reported bilateral increase of oxygenation in the frontal lobes while participants accomplished the tasks. Both studies which investigated blood changing patterns in the frontal lobes in aging found a tendency of activation decline in these regions. Study 8 pointed to a reduction in frontal lobes activity generated by alcohol ingestion. The experiment reported in study 10, which compared children and adolescents' performance while solving the Stroop test, suggested a higher recruitment of dorso-lateral pre-frontal cortex in the older participants to maintain a high level of performance. Cognitive flexibility processing, tested in study 11 by the application of the TMT, revealed higher activation in frontal regions for the resolution of Part B of the test than of Part A, which is simpler to be solved. Finally, study 13 reported an increase in oxygenation mainly in the frontal region in the left hemisphere in healthy children, while an imbalance between oxygenation and deoxygenation was found in the children with a developmental attention-deficit hyperactivity disorder. Thus, results brought by all the studies here reported demonstrated the involvement of frontal cortical regions in the processing of the EF they had selected.

DISCUSSION

The review presented in this article has characterized studies developed on EF processing analyzed by the use of fNIRS. As it is generally the case with neuroimaging studies on cognitive processing (for instance, as in the fMRI study developed by Davidson et al., 2006 on EF), the main aim of the majority of fNIRS studies on EF published up to date has been to localize the functional correlates of EF. In addition, when it comes to sampling features, the samples under analyses have been composed mainly by healthy young adults; moreover, the participants' education level has not always been specified in the studies. Regarding the already known education influence on EF processing (Plumet, Gil and Gaonac'h, 2005), it would be important to specify the control of this variable or its manipulation in fNIRS studies. From the clinical participants, only psychopathologies have been investigated, more specifically individuals with schizophrenia. Thus,

there is a lack of studies on EF processing in other clinical populations with neurological disorders (e.g., stroke, dementia, Parkinson). These studies could be very important for bringing evidence on brain circuitry during executive tasks in the neuropsychological assessment of neurological patients, such as right-brain-damaged and closed head injured people, generally characterized by disexecutive syndrome (Chevignard, Taillefer, Picq and Pradat-Diehl, 2008; Griffin et al., 2006).

Regarding EF components, the most investigated processes have been initiation and verbal planning inherent to verbal fluency tasks and interference to inhibition assessed by the Stroop test. Both tasks are commonly used as EF assessment tools (Lezak et al., 2004; Strauss, Sherman and Spreen, 2006). So they are representative instruments to be used in association to neuroimaging techniques such as fNIRS. The analyses of the studies here reported point to the necessity of a clearer investigation on the constructs which compose EF. Two articles were excluded from the analyses because they did not clearly elect one specific component. Yet, they investigated participants' performance in a specific task whose resolution indirectly recruited an executive component. Thus, it seems that research has to further investigate executive constructs, in order to propose a more refined categorization and classification.

A closer analysis of the data collected from the selected studies suggests a great concern of the authors in validating the technique, since its application for investigating brain functioning during cognitive tasks performance is very recent, particularly when it comes to the study of EF. The concern with the validation of the technique can as well be observed by the amount of studies which simultaneously used fNIRS and fMRI in order to check whether results from both data collection sources would corroborate one another (Sassaroli, Martelli and Fantini, 2006).

Another relevant aspect mentioned in the great majority of the studies here reported is the suitability of the application of fNIRS for the investigation of frontal lobes involvement in cognitive tasks, namely EF processing, the topic of this article. However, a characteristic detectable in all studies is that they have not focused on frontomedial and some other subareas in the frontal lobes due to limited depth penetration (Villringer and Chance, 1997) and to the anatomy of these areas, and only one focused on temporal regions, which may as well impose higher levels of difficulty for spatial analyses due to biological features of these areas. This has been the case due to fNIRS low spatial resolution, as previously mentioned. Therefore, the results of fNIRS investigations of

specific functions generally associated to ventrolateral and orbitofrontal regions of prefrontal lobes, although already focused by fMRI studies (Wagner, Maril, Bjork and Schacter, 2001), should be considered with precaution.

CONCLUSION

The construct of EF has a crucial importance in cognitive processing. Due to their relevance for a better understanding of underlying processes related to human cognition, further neuroimaging research should study and specify a wider array of their constructs or subcomponents. To overcome spatial resolution limitations of fNIRS to investigate some of these functions, a concomitant use of this technique with fMRI could represent an important alternative, which has been the case in several cognitive studies. In this way, fNIRS findings could be combined with fMRI higher spatial resolution, which is crucial in order to investigate brain correlates of each executive component.

Despite its limitations, evidence brought by fNIRS studies on human cognition has shown its validity as a neuroimaging technique sensitive enough to monitor functional brain metabolism in cognitive processing. It represents a potential and promising tool for an increasing and deeper investigation of human cognition, including its executive components.

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Recebido em: 31/07/2008. Aceito em: 08/09/2008.

Autores:

Yves Joanette – Professor and Researcher of the Department of Medicine, University of Montreal, and Director of Research of the Centre de Recherche, Institut Universitaire de Gériatrie de Montréal (CRIUGM), Quebec, Canada.
 Ana Inés Ansaldi – Professor and Researcher of the Department of Medicine, University of Montreal, and Laboratory Director of the Centre de Recherche, Institut Universitaire de Gériatrie de Montréal (CRIUGM), Quebec, Canada.
 Rochele Paz Fonseca – Professor and Researcher of the Department of Psychology, Pos-Graduation Program of Psychology (Human Cognition), Pontifícia Universidade Católica do Rio Grande do Sul (PUCRS), Brazil.
 Christian Haag Kristensen – Professor and Researcher of the Department of Psychology, Pos-Graduation Program of Psychology (Human Cognition), Pontifícia Universidade Católica do Rio Grande do Sul (PUCRS), Brazil.
 Lilian Cristine Scherer – Professor and Researcher of the Department of Linguistics and Literature (Reading and Cognition), Universidade de Santa Cruz do Sul (UNISC), Brazil.
 Maria Alice de Mattos Pimenta Parente – Professor and Researcher of the Department of Psychology, Universidade Federal do Rio Grande do Sul (UFRGS), Brazil.

Corresponding Author:

YVES JOANETTE
 4565 ch. Reine-Marie,
 Montréal, Québec, Canada H3W 1W5
 Tel.: (514) 340-3540, extension 4767 – Fax: (514) 340-3530
 E-mail: yves.joanette@umontreal.ca