1   **A N400 Event-Related Potential Elicitation Paradigm for Canadian French**

2   **Speakers**

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13

Abstract

15   The N400 event-related brain potential (ERP) can be used to evaluate language comprehension,

16   and may be a particularly powerful tool for the assessment of individuals who are behaviourally

17   unresponsive. This study presents a set of semantic violation sentences developed in Canadian

18   French and characterizes their ability to elicit an N400 effect in healthy adults. A novel set of 100

19   French sentences were created and normed through two surveys that assessed sentence cloze

20   probability ($n = 98$) and semantic plausibility ($n = 99$). The best 80 sentences (40 congruent; 40

21   incongruent) were selected for the final stimulus set and tested for their ability to elicit N400 effects

22   in 33 French-speaking individuals. The final stimulus set successfully generated an N400 effect

23   in the grand-average across all individuals, and in the grand-average within age groups (young,

1 middle-age, and older adults). On a single-subject level, the final stimulus set elicited N400 effects

2 in 76% of the participants. The feasibility of using this stimulus set to assess semantic processing

3 in behaviourally unresponsive individuals was demonstrated in a case example of a French

4 individual in a disorder of consciousness. These sentences enable the inclusion of Canadian

5 French speakers in this simple assessment of language comprehension abilities.

6

7 **Keywords** N400 ERP component, Cloze probability, Semantic plausibility rating, Canadian

8 French N400 elicitation paradigm, Canadian French

9

1. Introduction

11 Event-related potentials (ERPs) are electrophysiological responses to sensory, cognitive or

12 motor stimuli, and provide a non-invasive means of evaluating brain functioning. Through well-

13 crafted experimental designs, ERPs have been used to meaningfully assess cognitive processes

14 such as attention (Li et al., 2015; Näätänen, 1990), memory (Paller et al., 1987), semantic

15 processing (Connolly et al., 1992; Kutas & Van Petten, 1998) and psychometric intelligence

16 (Schafer, 1985; Stough et al., 1990). While they have been widely used in healthy populations,

17 ERPs are particularly powerful as a tool for evaluating the cognitive functions of individuals who

18 are unable to produce the behavioural responses required to complete standardized cognitive

19 assessment tests. As responses are recorded directly from the brain, the use of the ERPs for

20 cognitive assessment bypasses all requirements for physical or verbal responses and can

21 theoretically be used to assess individuals with the highest degrees of impairment. ERPs have

22 been used for cognitive assessment in individuals with cerebral palsy (Alcaide-Aguirre et al., 2017;

23 Byrne et al., 1995), Alzheimer's disease (Lai et al., 2010; Lee et al., 2013) and those who have

suffered a stroke (D'Arcy et al., 2003). Previous studies have also provided evidence that ERPs

can be used to assess consciousness in unresponsive individuals with disorders of consciousness,

such as unresponsive wakefulness syndrome (UWS) (Risetti et al., 2013; Rodriguez et al., 2014).

The N400 is an ERP component that is an index of the difficulty of retrieving stored

conceptual knowledge associated with an item in semantic memory (See Kutas & Federmeier,

2011 for a review). It has been successfully used to assess the current status of semantic memory

across many domains (e.g. words, pictures, sounds), and is commonly used to assess word

comprehension. Neurophysiologically, the N400 reaches its peak amplitude approximately 400

ms after stimulus onset at midline central or parietal sites, with a larger amplitude observed when

an item is less expected in a particular context relative to a item that is more expected (Kutas &

Hillyard, 1980; 1984). Although interpretations of the N400 vary, it is clear that the response

reflects higher level processing involving attention and language comprehension skills. In the

context of word comprehension, the N400 effect can be elicited through multiple experimental

paradigms, classically: 1) word-word priming paradigms, wherein word pairs that are semantically

congruent and semantically incongruent are presented to the participant; and 2) semantic violation

sentences paradigms, which consist of sentences wherein the terminal word is either semantically

congruent or semantically incongruent (e.g. "The pizza was too hot to sing"). These paradigms

can elicit N400s through both auditory and visual modalities, though the characteristics of the

evoked waveforms are slightly different. Auditory N400 tend to begin earlier, last longer, and

have a slightly more frontal and less right-biased topography (Kutas & van Petten, 1994). There

is ample evidence that the N400 component evoked through both modalities is fundamentally

related to the strength of the expectation produced by the context in which a word is found, and

that the context provided by discourse results in a larger N400 than a sentence (Van Berkum et al.,

1   1999), which in turn is larger than word-word priming (Ziegler et al., 1999). Previous studies have

2   used the presence of an auditory N400 effect to establish cognitive processing, and thus a high

3   level of consciousness, in behaviourally unresponsive patients (Risetti et al., 2013; Rodriguez et

4   al., 2014).

5   The overarching goal of this study was to develop an experimental paradigm that could

6   assess the language comprehension of individuals with minimal behavioural responsiveness in

7   Montreal, Canada, where a large proportion of the population is Francophone. As most

8   behaviourally unresponsive individuals have unreliable visual fixation, we focused on the

9   development of an auditory N400 paradigm. Previous studies have used the N400 effect to assess

10   language comprehension in French; these have employed experimental paradigms ranging from

11   the processing of written syllables (Chetail et al., 2012) to syntactic processing of auditory

12   sentences in healthy young adults (Isel et al., 2007). However, as these paradigms do not reliably

13   elicit an N400 effect response in healthy adults (Rohaut et al., 2015), we focused on a semantic

14   violation sentence paradigm to maximize the likelihood of generating an N400 in our target

15   population. We conducted an extensive search for a set of normed and validated sentences that

16   could elicit an N400 effect in a Francophone-dominant population. While such sentences have

17   been developed in English (visual; Kutas & Hillyard, 1980), Italian (visual; Angrilli et al., 2002),

18   Dutch (visual and auditory; Hagoort & Brown, 2000), and German (visual and auditory; Friederici

19   et al., 1996), none existed for Canadian French. A set of European French semantic violation

20   sentences exists (Robichon et al., 1996); however, they were normed in France — thus not

21   representative of the Canadian French patterns of expectation — and had never been evaluated for

22   their ability to elicit an N400 effect. Moreover, the existing N400 English sentences cannot simply

23   be translated into French, as the semantic characteristics vary between languages. Thus, the

specific aims of this study were 1) to create and norm a set of Canadian French sentences with high semantic congruency and incongruency; 2) to assess the ability of the best sentences from aim 1 to generate an N400 effect in healthy Canadian dominant French speakers; and 3) to test the feasibility of using these sentences to assess the language processing abilities of an individual in a disorder of consciousness.

2. PHASE 1: SENTENCE CREATION AND NORMING

2.1 Materials and Method

2.1.1 Sentence Creation

Sentence creation was seeded from a list of French consonant-initial monomorphemic singular nouns. French vowel-initial words are affected by what is called "liaison" – a pronunciation of a latent word-final consonant immediately before a following vowel sound. By only including consonant-initial nouns, we avoided the liaison and ensured that the last word in the continuous speech signal had a clear physical marker that could be used to align the ERP waveform to the onset of the sentence-final word. Words were matched on the following linguistic and psycholinguistic variables: frequency, length (number of phonemes and syllables), imageability, phonological neighbours, and uniqueness point (Desrochers, 2006; OMNILEX database of French words). The words from this list became the terminal words of the prospective N400 sentences, thus ensuring comparability. The word-final semantic violation version of the paradigm was chosen because it is the most widely used version of the N400 paradigm in the ERP literature. The characteristics of the linguistic and psycholinguistic variables for the terminal words of both groups of sentences are presented in Table 1. One hundred sentences were generated, equally divided into two groups: semantically congruent and semantically incongruent. Congruent sentences had a mean length of 7.9 words (range: 5-12 words) and were designed to lead the

1 listener to correctly predict the final word (e.g. Paul aime le pepperoni sur sa pizza. "*Paul likes*

2 *pepperoni on his pizza*"). Incongruent sentences had a mean length of 8.4 words (range: 5-14

3 words) and were designed to violate the listener's expectation of the terminal word (e.g. Elle est

4 allée à la boulangerie pour acheter une miche de veste. "*She went to the bakery to buy a loaf of*

5 *vest*").

	Congruent (n = 50)	Incongruent (n = 50)
Grammatical Gender	26 F / 24 M	17 F / 33 M
Mean Subjective Frequency Rating	5.15 (range: 3.14-6.16)	4.70 (range: 2.8-5.8)
Mean Film Frequency (per million)	41.41 (range: 15.18-101.51)	36.22 (range: 15.06-122.05)
Mean # Phonemes	4.94 (range 4-7)	4.94 (range 4-8)
Mean # Syllables	1.82 (range 1-3)	1.88 (range 1-3)
Mean Imageability Rating	5.51 (range 5-6.23)	5.54 (range 5-6.16)
Mean # Phonological Neighbours	4.02 (range 0-12)	4.84 (range 0-11)
Mean Uniqueness point	4.82 (range 3-7)	4.94 (range 4-7)

6 *Table 1. Linguistic and psycholinguistic variables for sentence final words for the 100 sentences*

7 *for Phase 1*

8 **2.1.2   Sentence Norming**

9   The acceptability norms of the prospective N400 sentences were assessed by establishing

10 the cloze probability and the semantic plausibility of each sentence.   Cloze probability was

11 assessed through a sentence completion survey, where respondents were provided the sentences

12 with the terminal word omitted and asked to fill in the missing word. Semantic plausibility was

13 assessed by providing respondents with full sentences, and asking them to rate them on a 5-point

14 Likert scale, with 1 corresponding to "La phrase est tout à fait logique" ("*The sentence makes*

15 *perfect sense*") and 5 corresponding to "La phrase est complètement illogique" ("*The sentence*

16 *makes no sense at all*"). To confirm French language dominance, participants also completed a

17 language assessment questionnaire (Questionnaire des antécédents langagiers- version courte)

1   (Sabourin et al., 2016); those who did not have French as their dominant language were excluded

2   from all analyses.

3

2.1.3   Participants

5   We received 198 completed surveys; one was excluded for failing the French dominance

6   questionnaire. The remaining 197 surveys consisted of data from dominant French-speaking

7   adults (148 female) ranging in age between 18 and 87 years (mean: 34.4, SD: 19) Recruitment

8   occurred through a wide variety of academic and community venues to attempt to capture diverse

9   educational backgrounds and a wide range of ages. Participants were not compensated for their

10   time and surveys were anonymous. Hardcopies of the surveys were distributed to participants in

11   undergraduate and graduate classes at a local university, left in waiting rooms in local hospitals,

12   and distributed through community networks. Approximately two thirds of the surveys in our final

13   sample were returned from an academic setting and one third from a community setting. The study

14   was approved by the research ethics board of the Centre for Interdisciplinary Research in

15   Rehabilitation of Greater Montreal (CRIR).

16

2.2   Results

18   <u>Participant Characteristics</u>

19   A total of 99 (71 F) participants aged 18 to 82 (mean: 33.7, SD: 17.4) completed the

20   Semantic Plausibility survey. Of these 99, 84 (86.6%) were born in the province of Québec, 2

21   (2.1%) were born in a Canadian province other than Québec, and 11 (11.3%) were born outside of

22   Canada (information was missing for 2 participants). All participants had completed secondary

23   school, 26 (26.8%) had an undergraduate or graduate degree, and 48 (49.5%) were completing an

1 undergraduate degree. A total of 98 (77 F) participants aged 18 to 87 (mean: 34.7, SD: 19.8)

2 completed the Sentence Completion survey. Of these 98, 77 (81.1%) were born in the province of

3 Québec, 4 (4.2%) were born in a Canadian province other than Québec, and 14 (14.7%) were born

4 outside of Canada (information was missing for 3 participants). All participants had completed

5 secondary school, 34 (35.1%) had an undergraduate or graduate degree, and 49 (50.5%) were

6 completing an undergraduate degree.

7

8 Prospective N400 Sentences Characteristics

9   Prospective N400 sentences designed to be semantically congruent were considered

10 acceptable if a) more than 80% of survey respondent ranked their semantic plausibility either 1 or

11 2, and the average semantic plausibility rating was under 2; and b) if the cloze probability for the

12 target word equalled or exceeded 80%. Prospective N400 sentences designed to be semantically

13 incongruent were considered acceptable if a) more than 80% of survey respondents ranked their

14 semantic plausibility either 4 or 5, and the average semantic plausibility rating was over 4; and b)

15 if the cloze probability of the target word was 0% and the survey respondent supplied a non-target

16 word that had a cloze probability of over 80%.

17   A total of 86 sentences met the acceptability criteria. Of these, the 80 with the highest

18 congruent ratings (40) and the highest incongruent ratings (40) were selected to create the final

19 stimulus set of N400 sentences. The linguistic and psycholinguistic characteristics of the terminal

20 words sentences included in the final set are listed in Table 2.

	Congruent (n = 40)	Incongruent (n = 40)
Grammatical Gender	22 F / 18 M	13 F / 27 M
Mean Subjective Frequency Rating	5.21 (range: 3.14 - 6.16)	4.69 (range: 3.30 - 5.8)
Mean Film Frequency (per million)	42.19 (range: 15.18 - 101.51)	36.04 (range: 15.06 - 98.49)

Mean # Phonemes	4.9 (range 4 - 7)	5.03 (range 4 - 8)
Mean # Syllables	1.8 (range 1 - 3)	1.93 (range 1 - 3)
Mean Imageability Rating	5.49 (range 5 - 6.23)	5.57 (range 5.12 - 6.16)
Mean # Phonological Neighbours	3.88 (range 0 - 12)	4.8 (range 0 - 11)
Mean Uniqueness point	4.80 (range 3 - 7)	5.03 (range 4 - 7)

Table 2. Linguistic and psycholinguistic variables of sentence final words for the final 80 sentences

Incongruent sentences had a mean semantic plausibility rating of 4.6, with 90% of participants ranking the semantic plausibility as 4 or 5. The mean cloze probability for the target words of incongruent sentences was 0%, and each had a non-target word that would logically end the sentence with a mean cloze probability of 94%. Incongruent sentences ranged from 6 to 14 words, with a mean word length of 8.4.

Congruent sentences had a mean semantic plausibility rating of 1.2, with 94% of participants ranking the semantic plausibility as 1 or 2. The mean cloze probability for the terminal word of these sentences was 91%. Congruent sentences ranged from 5 to 12 words, with a mean word length of 7.9.

The complete final stimulus set of N400 sentences is presented in Appendix A.

3. PHASE 2: N400 EVENT-RELATED POTENTIAL VALIDATION

In the second phase of this study, the final stimulus set of N400 sentences were presented to individuals dominant in the French language while a high-density electroencephalogram (EEG) was recorded. EEG signals were analyzed for the presence/absence of an N400 event-related potential in response to incongruent and congruent sentences.

3.1 Materials and Methods

3.1.1 Participants

A total of 33 dominant French-speaking individuals (22 F, age 17–79 years) with normal hearing were recruited for this study. Each participant was assigned to one of three age-groups: 1) Group 1 - young adult (13 participants; 8 female; age 17–24 years); 2) Group 2- middle-age (12 participants; 10 female; age 25–54 years); 3) Group 3 - older adult (8 participants; 4 female; age 55–79 years). All participants completed secondary school, 9 (27.27%) had an undergraduate or graduate degree and 12 (36.36%) participants were completing an undergraduate degree. Participants were excluded if they had any developmental, acquired or degenerative neurological deficits, including epilepsy, traumatic brain injury and Alzheimer's disease. Language dominance was established using the Questionnaire des antécédents langagiers- version courte (Sabourin et al., 2016); no participants were excluded as a result of failing the language dominant test.

3.1.2 Stimulus Presentation

Each of the 80 sentences in the final stimulus set was recorded by a native Canadian French speaker in mono-mode using the software Audacity (version 2.1.0). Auditory files were denoised, converted to stereo, and normalized for intensity. The onset time (ms) of the first, second, penultimate and terminal words of each sentence were extracted using Praat speech analysis software (version 6.0.14). Each auditory file and its associated markers were imported into Presentation (2018) software. The final stimulus presentation consisted of sentences presented in a random order with an inter-sentence interval of 3 seconds.

3.1.3 Electroencephalographic Recording and Pre-processing

High-density electroencephalography (hdEEG) was recorded from each participant using a 128-channel system from Electrical Geodesics Incorporated (EGI), while the auditory stimulation paradigm was presented through stereo speakers located on either side of the

1 participant. Prior to data collection, electrode impedances were reduced to below 50 kΩ, as per

2 manufacturer recommendations. EEG data were recorded at a frequency of 1000 Hz with no online

3 filters and referenced to the vertex. Participants were instructed to minimize movement and listen

4 to each sentence with their eyes open, while fixating on a picture of a nature scene. After each

5 sentence, participants were asked to press a YES or NO button on a button-box to indicate whether

6 the sentence made sense to them or not. EEG corresponding to sentences with an incorrect

7 behavioural response were removed from subsequent analyses.

8 After the experiment, EEG signals were bandpass filtered between 0.1 and 50 Hz and re-

9 referenced to an average reference. An investigator experienced in reading electroencephalograms

10 visually inspected the data to reject epochs and channels with noise or non-physiological artifacts.

11 An independent component analysis (ICA) was conducted to identify and remove artifacts related

12 to eye blinks and eye movements. The preprocessed EEG of all 33 participants were included in

13 the event-related potential analysis.

14 **3.1.4 Event-Related Potential Analysis**

15 Event-related potential analysis was conducted in Brain Vision Analyzer 2 using the pre-

16 processed EEG data from each participant. EEG data were segmented 200 ms prior to and 800 ms

17 following the onset of the final word of each sentence, baseline corrected, and divided into two

18 groups corresponding to congruent and incongruent sentences. Segments that contained significant

19 noise (e.g. $\pm$ 100 µV cut-off) were excluded from subsequent analyses using the artifact rejection

20 algorithm within Brain Vision Analyzer 2. EEG data were then averaged across each electrode to

21 generate subject-averaged waveforms for congruent and incongruent sentences. For each

22 participant average waveform, difference waves were generated on 3 electrode sites (Fz, Cz, Pz),

23 as recommended in best practice guidelines for recording and quantifying N400 ERPs (Duncan et

al., 2009), where maximal amplitudes are expected at midline central or parietal sites and smaller amplitudes at frontal sites. Grand average waveforms were produced for congruent and incongruent averages at each site, first for all 33 participants and subsequently for the three age groups. Serial *t*-tests were then applied on the difference wave between congruent and incongruent grand average sentences to assess whether a significant N400 response was generated at a group-level (Perrin et al., 2006). The difference between congruent and incongruent averages was deemed significant when the p-value was less than 0.05 for at least 40 ms.

3.2   Results

3.2.1   Participants Correctly Identified the Congruent and Incongruent Sentences

The participants' behavioural responses to whether or not the sentences "made sense" were tracked using a YES/NO button box. On average, participants generated an erroneous response to 0.98 of the total 80 sentences. The behavioural response to the ERP task did not vary significantly across age groups: young adults on average generated 0.54 erroneous responses to the 80 sentences (0.58% error rate); middle aged adults generated 1.08 erroneous responses (0.135% error rate); and older adults generated 1.13 erroneous responses (0.14% error rate). In summary, across all three age groups, participants were able to accurately identify the sentences intended to be congruent and sentences intended to be incongruent.

3.2.2   The Final Stimulus Sentences Set Generated N400 Event-Related Potentials

The final stimulus sentence set generated a significant N400 effect in the grand average across all participants (Figure 1). The N400 had the greatest amplitude at Cz and was significant

1   272–632 ms after the onset of the terminal word. An N400 effect was also significant at Pz 372–

2   580 ms after the onset of the terminal word.

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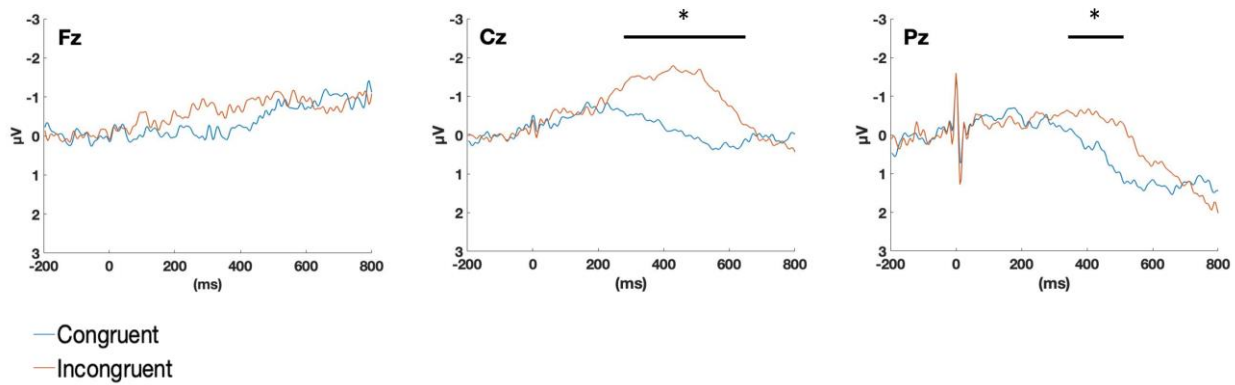
Figure 1: Grand average waveforms across all participants (n = 33). Orange = average of all incongruent sentences (40); Blue = average of all congruent sentences (40). N400 ERPs are present in Cz and Pz; timepoints where the waveform differences (congruent – incongruent) are significant are marked *.

4   **3.2.3   The Final Stimulus Set Generated N400 ERPs Across All Age Groups**
5
6   N400 effects were analyzed within each age group to determine if the response to the

7   sentence stimulus set varied with age. Significant N400 effects were observed for all age groups

8   (Figure 2). The waveforms were significant for group 1 at Fz (252–486 ms) and Cz (254–632 ms);

9   group 2 at Cz (388–572 ms) and Pz (444–584 ms); and group 3 only at Cz (384–440 ms).
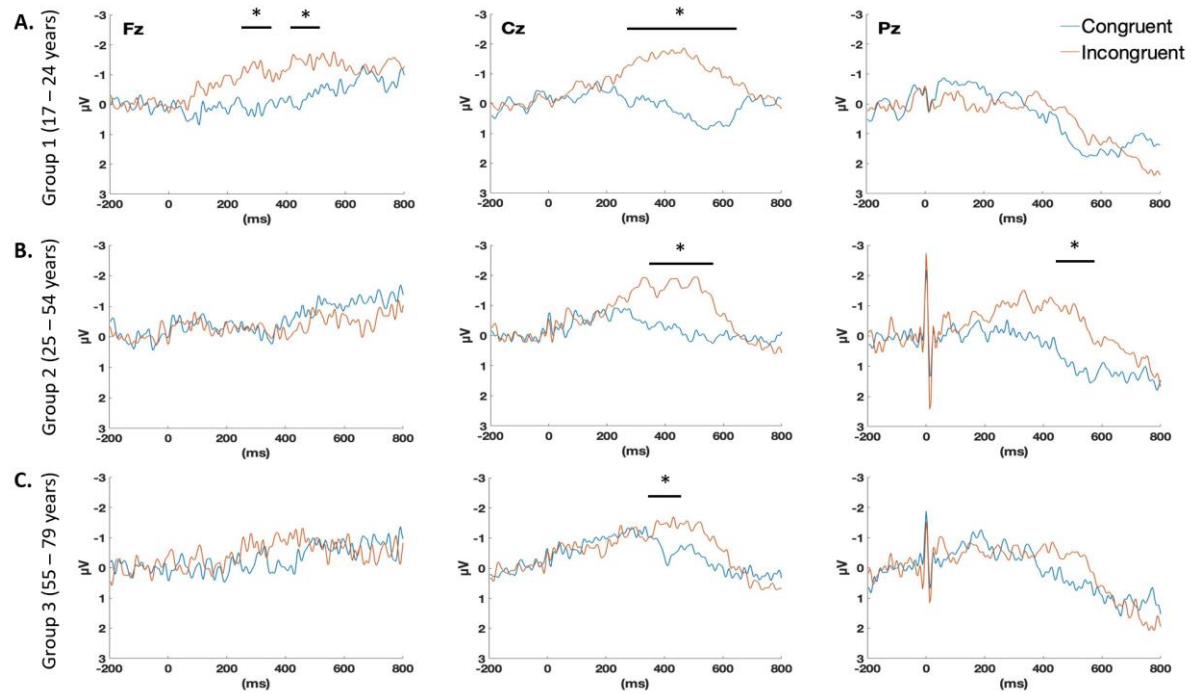
10

Figure 2: N400 event-related potentials across three age groups: A = group 1 (young adults; n = 13); B = group 2 (middle age; n = 12); C = group 3 (older adults; n = 8). Orange = incongruent sentences, Blue = congruent sentences; timepoints of significant are marked *.

1

3.2.4   Individual Responses to Sentences Varied Between Age Groups

Serial *t*-tests were applied to the average waveforms for congruent and incongruent sentences within each individual to determine whether or not N400 effects were detected on a single-subject level. Overall, 8 of the 33 participants did not show significant N400 effects to the sentences. Across age groups, 2/13 individuals (15%) did not generate N400 effects in group 1; 2/12 individuals (17%) did not generate N400 effects in group 2; and 4/8 individuals (50%) did not generate N400 effects in group 3 (Figure 3). Within the 25 participants who generated N400 effects, the characteristics of the average waveform varied between individuals, with 11 participants exhibiting an anterior-dominant waveform (i.e. significant N400 effects at Fz and/or

1   Cz sites), and 14 participants exhibiting a posterior-dominant waveform (i.e. significant N400

2   effects at Cz/Pz sites) (Figure 3).
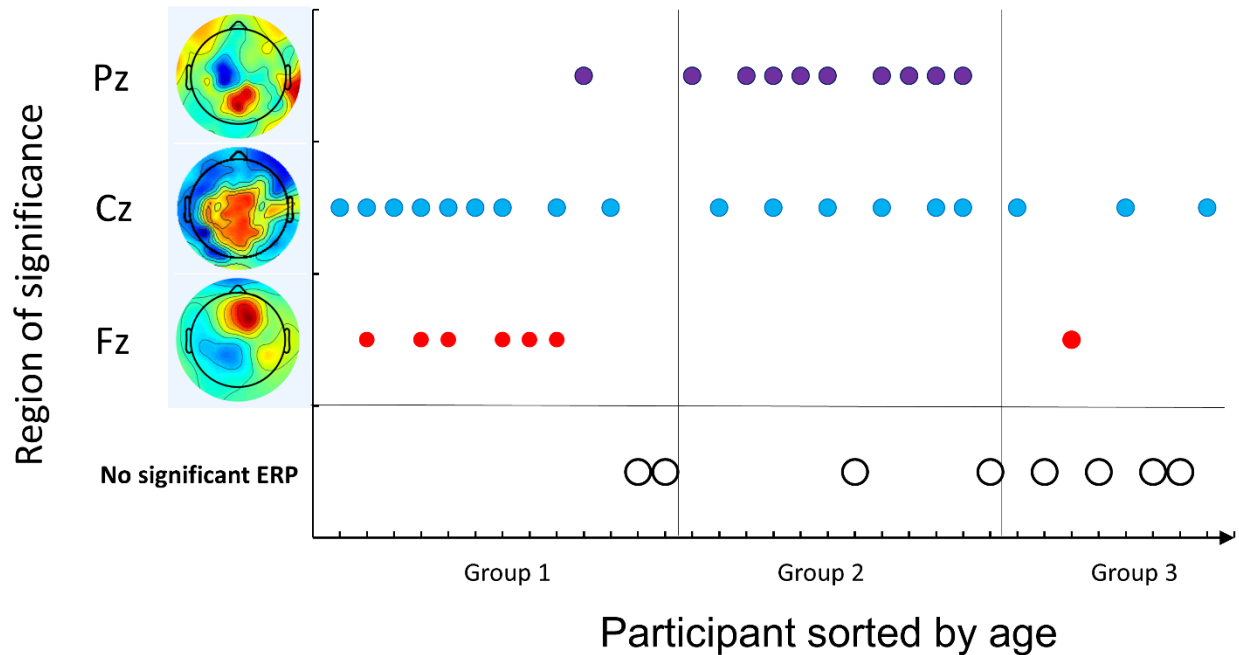
3

4   *Figure 3: Locations of significant N400 effects of all participants, sorted by age.* The N400 effect
5   in group 1 (young adults) are primarily located at Fz (red) and Cz (blue); N400 effects in group 2
6   (middle-age) are primarily located at Cz (blue) and Pz (purple).). The N400 effects in group 3
7   (older adults) are primarily located at Cz (blue). Individuals who did not show a significant ERP
8   are indicated in white. Some participants are represented by more than one coloured dot.
9

10   The largest proportion of individuals who did not generate N400 responses were in age

11   group 3. Since visual and auditory N400s effects have been reported in older adults (i.e. 60+ years)

12   in the literature (Wlotko et al., 2010), we conducted a secondary analysis of the average waveforms

13   for this subgroup (Figure 4). While only 2/5 individuals who were 60 years or older generated

14   N400 effects in the individual average, the grand average of this subset of participants from group

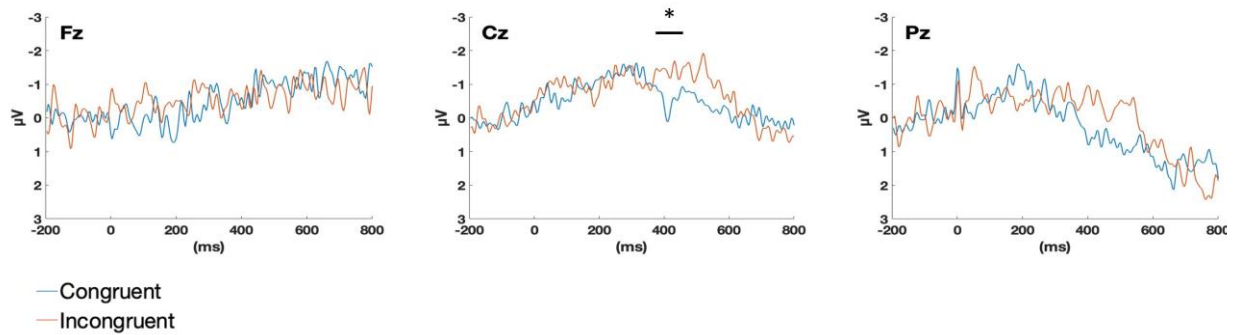15   3 shows a significant N400 effect at Cz between 396–436 ms.

Figure 4: Grand average waveforms for participants 60+ (n = 5). A significant N400 effect is present in Cz.

4.   CASE APPLICATION: DISORDERS OF CONSICOUSNESS

4.1   Materials and Methods

To demonstrate the feasibility for the final sentence stimulus set to generate an N400 effect in minimally-responsive individuals, the sentences were tested on a patient in a disorder of consciousness, recruited as part of a separate research study (McGill University Health Center Research Ethics Board study ID 15-996-MP-CUSM). The participant was a 75-year old female, native Canadian French speaker who had suffered a stroke resulting in a subarachnoid hemorrhage. Before the study, next of kin provided written informed consent. The participant's level of consciousness was assessed using the Coma Recovery Scale-Revised (CRS-R) – a validated measure of awareness, and the current gold standard of assessing disorders of consciousness (Giacino et al., 2004). Immediately prior to EEG testing, the participant had a Coma Recovery Scale-Revised (CRS-R) score of 5, consistent with a diagnosis of unresponsive wakefulness syndrome, and indicating that the patient was not conscious. The participant was outfitted with a 128-channel EEG system and listened to the final sentence stimulus set played through noise-canceling headphones under three conditions: 1) pre-anesthesia rest; 2) exposure to anesthesia; and 3) recovery from anesthesia.   As long-latency ERPs associated with consciousness have

1   paradoxically been observed in patients with a diagnosis of persistent unresponsive wakefulness

2   syndrome (Fischer et al., 2010; Kotchoubey, 2005), we use anesthesia to test reliability of observed

3   ERPs in brain-injured individuals. If an observed N400 was indeed a marker of language

4   processing, we would expect it to disappear when an individual is exposed anesthesia, and to return

5   upon emergence from anesthesia. The protocol is detailed in full in (Blain-Moraes et al., 2016).

6   Briefly, after the pre-anesthesia recording, propofol anesthesia was delivered through a target-

7   controlled infusion pump targeting an effect site concentration of 2 μg/mL. The N400 sentences

8   were played once a steady-state concentration at the effect site was achieved. Propofol was then

9   discontinued, and the sentences were repeated once the effect site concentration dropped below

10 0.5 μg/mL. After recording, EEG was pre-processed according to the procedure described in

11 Section 3.1.3. The cleaned EEG was segmented 200 ms prior to and 800 ms following the onset

12 of the terminal word of each sentence, and average waveforms for incongruent and congruent

13 sentences were generated across electrodes Fz, Cz and Pz.

14 **4.2   Results**

15 In this case example, the final French sentence stimulus set elicited an N400 effect during

16 the pre-anesthesia rest condition in the patient with a disorder of consciousness (Figure 5A). There

17 was no visual difference between congruent and incongruent sentence average waveforms when

18 the patient was exposed to anesthesia, consistent with a patient who is unconscious (Figure 5B).

19 Upon recovery from anesthesia, a difference waveform reappeared that was consistent with an

20 N400 effect (Figure 5C). The appearance and disappearance in N400 waveforms across three

21 conditions suggest that the waveform is not an artifact, nor a spurious phenomenon, but the result

22 of conscious processing of the sentence stimuli. In this particular case example, we cannot draw

23 a firm conclusion about the presence or absence of consciousness in the patient, as care was

1   withdrawn, and the patient died a week after the EEG recording. However, this case demonstrates

2   the *feasibility* of using the final sentence stimulus set to elicit N400 effects in a behaviourally

3   unresponsive individual.

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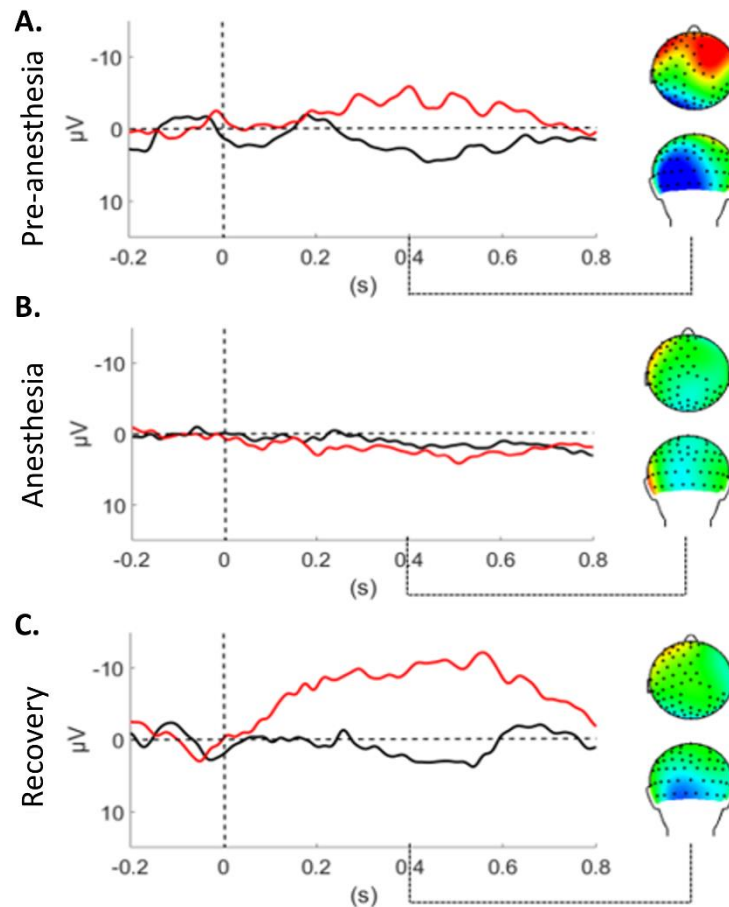
5 **Figure 5: Average EEG waveforms for congruent (black) and incongruent (red) sentences**
6 **in a patient in a disorder of consciousness.** A significant N400 effect is present at Pz during pre-
7 anesthesia rest (A), disappears when the patient is exposed to anesthesia (B), and reappears upon
8 recovery (C), though it does not reach significance.
9

10   **5. DISCUSSION**

11   The current study presents the development and characterization of a set of auditory

12   sentence stimuli that successfully elicit N400 effects in dominant French speakers. A final set of

13   40 congruent and 40 incongruent French sentences were presented. The two sentence groups were

1   matched for linguistic and psycholinguistic characteristics including grammatical gender,

2   subjective frequency rating, film frequency, number of phonemes and syllables, imageability,

3   phonological neighbours and uniqueness point. The auditory sentence stimuli elicited a significant

4   N400 effect in the grand average of healthy adults; significant N400 effects were also evident in

5   the grand averages within groups of young, middle-aged and older adults. The N400 effect was

6   dominant in Cz and Fz for the young adult group, as expected with auditory evoked N400s (Kutas

7   & Federmeier, 2011), while the effect was dominant in Cz and Pz for the middle-aged adults. On

8   an individual-subject level, the sentence stimuli did not generate N400 effects across all

9   individuals; individuals who did not show single-subject N400s were predominantly amongst the

10   older adults.

11   This study also demonstrates the feasibility of using the presented set of sentences to elicit

12   N400 effects in individuals with minimal behavioural responsiveness; in a case example of a

13   dominant-French speaking patient with a disorder of consciousness, the set of sentences elicited

14   N400 effects in a baseline resting condition, which disappeared when the patient was exposed to

15   anesthesia, and appeared to recover after the effects of anesthesia. These results belie the patient's

16   diagnosis of unresponsive wakefulness syndrome and suggest the presence of semantic processing

17   ability despite her behavioural unresponsiveness. The sentences developed in this study join a

18   growing set of stimuli intended to elicit N400 effects in a variety of languages (Angrilli et al.,

19   2002; Friederici et al., 1996; Hagoort & Brown, 2000; Kutas & Hillyard, 1980), and enable the

20   inclusion of dominant Canadian French speakers in semantic processing research. Moreover, they

21   constitute an accessible tool that can potentially be used to assess the language capabilities of

22   dominant Canadian French-speaking individuals with minimal behavioural responsiveness,

1   including those who have experienced a stroke, a traumatic brain injury, or who have a disorder of

2   consciousness.

3   While the presented sentences reliably generated grand-average N400 ERP effects across

4   all healthy adults and within each age group, the lack of a consistent presence of single-subject

5   N400 effect limits the usefulness of this sentence stimuli for individual assessment, especially in

6   older adults. Half of the older adults (50%) who participated in our study did not demonstrate a

7   significant N400 effect in response to the sentence stimulus set, in contrast to the younger two

8   groups, where ERPs were absent in 15% and 17% of individuals, respectively. Transitioning from

9   childhood to adulthood involves the exponential increase of vocabulary and overall knowledge

10   which continues into late adulthood and aging. However, aging is also accompanied by a decline

11   in processing speed, working memory, inhibitory function, long-term memory, decrease in brain

12   structure size and white matter integrity (Park & Reuter-Lorenz, 2009) as well as decline in

13   semantic integration during sentence comprehension (Federmeier et al., 2010; Wlotko et al.,

14   2010). While theories such as the Scaffolding Theory of Aging and Cognition (STAC) provide an

15   account that integrates the development of complementary and alternative neural pathways to

16   achieve specific cognitive goals (Park & Reuter-Lorenz, 2009), more recent evidence from studies

17   using ERPs reveals that aging is associated with both quantitative and qualitative changes in

18   language processing, specifically with regard to comprehension (Zhu et al., 2017).   Our results

19   contribute to recent literature investigating semantic integration during auditory and visual

20   sentence comprehension across ages (Federmeier et al., 2010; Wlotko et al., 2010; Zhu et al.,

21   2017). Some studies have shown a decrease in auditory and visually evoked N400 amplitude and

22   reaction time with age (Federmeier et al., 2003; Gunter et al., 1992; Kemmotsu et al., 2012; Kutas

23   & Iragui, 1998; Wlotko et al., 2010), while other studies have shown reduced auditory evoked

N400 amplitudes in older individuals, but similar latencies across the younger and older participants (Federmeier et al., 2002, 2003). These findings have been reported on the group average; our results provide a more nuanced single-subject examination of this phenomenon, and suggest that the decreased N400 amplitude in older individuals may be a result of the higher proportion of this age group that do not produce significant N400 ERPs.

In spite of the lack of single-subject reliability, the set of French N400 sentences developed in this study shows substantial promise as a tool to investigate the language-processing abilities of dominant-French minimally communicative individuals. While the *absence* of an N400 effect does not necessarily indicate the absence of sentence comprehension, the *presence* of an N400 effect strongly suggests that these cognitive processes remain intact. Language processing is complex, multifaceted and depends on a number of cognitive systems and processes that work in tandem and with extraordinary speed. The presence of an N400 effect demonstrates that as words and sentences are processed in real time, linguistic features such as morphological and syntactic characteristics are accessed and meanings are computed, resulting in language comprehension. This can be powerfully used, for example, in the assessment of the level of awareness in patients with disorders of consciousness – a population with a misdiagnosis rate of over 40% (Schnakers et al., 2009). As illustrated in the case example presented in this study, individuals with unresponsive wakefulness syndrome (e.g. unconsciousness) can show N400 effects in response to these sentence stimuli, bringing the diagnosis into question and generating evidence for the need to conduct further tests. This is a relatively accessible test for many behaviourally unresponsive patients, where upwards of 50% present with conditions that are incompatible with magnetic resonance imaging (MRI) and related measures, including functional MRI (fMRI), diffusion tensor imaging (DTI) and susceptibility weighted imaging (SWI). The creation of these sentences

enables the inclusion of dominant Canadian French speakers in this simple assessment of language comprehension abilities, which is also relevant for other populations including stroke and traumatic brain injury.

The final sentence stimulus set presented in this study should be deployed for further research, keeping in mind certain limitations. First, EEG was recorded from participants who had their eyes open, and who were asked to generate a physical response to the sentences in order to maintain their focus and attention. In a pilot of this study, EEG was recorded from eight individuals who listened passively to the sentences with their eyes closed: the N400 effect was not present in any individual subject, nor in the grand average. These results can be explained by the large amount of alpha waves that are typically present in an eyes-closed condition which obscure many ERPs, and by subjective reports of progressive sleepiness and loss of attention over the course of the experiment. For optimal results, EEG should be recorded from participants under similar conditions; a situation that may not be possible to produce in some minimally-communicative individuals. Second, the sentences were normed in a population of individuals who spoke Canadian French, and audio recorded from an individual native to the province of Québec. Subtle linguistic differences across different geographic locations; in this case, the Quebecois accent of the speaker, may affect the translatability of these N400 sentences to French-speaking provinces outside of Canada. Finally, the topographic location of the peak N400 difference will not only vary with age (Figure 3), but also in response to the particular source and location of brain injury resulting in a patient's minimal responsiveness; when using these sentences to assess a patient's language comprehension, the N400 should be sought across many electrode sites, rather than focusing on the canonical N400 locations of Cz and Pz.

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4

5

Appendix A

				Semantic Plausibility		Sentence Completion		
#	**Sentence**	**Number of words**	**Target word**	**% of participants who answered 4-5**	**Average rating**	**Cloze probability for target**	**Cloze probability for other word produced**	**Other word produced**
1	Pour accrocher le cadre, Nicholas avait besoin d'un marteau et d'un navire.	14	navire	87.6%	4.52	0%	93.0%	clou
2	Dans la douche, il se lave la peau avec du teste.	11	teste	86.9%	4.52	0%	96.9%	savon
3	Elle est allée à la boulangerie pour acheter une miche de veste.	12	veste	92.0%	4.70	0%	100%	pain

Table title: Sentences with an incongruent word ending

4	Katie a mis le bouquet de fleurs dans un poisson.	10	poisson	87.9%	4.55	0%	81.6%	vase
5	Le cowboy a mis la selle sur le billet.	9	billet	92.8%	4.67	0%	97.9%	cheval
6	Le fermier ne veut pas traire sa grenade.	8	grenade	90.7%	4.60	0%	95.9%	vache
7	La nuit, Anik verrouille la poudre.	6	poudre	86.9%	4.49	0%	90.8%	porte
8	L'enfant se couche dans le cerveau.	7	cerveau	91.9%	4.75	0%	81.4%	lit, berceau, bassinet
9	Au parc, la fille se balance sur la chemise.	9	chemise	88.7%	4.58	0%	97.9%	balançoire
10	Autour de la taille, il porte une cabine.	8	cabine	90.9%	4.67	0%	99.0%	ceinture
11	Chloé boit son thé glacé avec une facture.	8	facture	84.6%	4.49	0%	87.6%	paille
12	Ils sont allés voir le nouveau film au moteur.	9	moteur	92.0%	4.71	0%	100%	cinéma
13	La petite fille s'est couchée dans son satellite.	9	satellite	80.8%	4.35	0%	93.8%	lit, berceau

14	Les oisillons sont prêts à partir du fromage.	8	fromage	88.9%	4.61	0%	92.8%	nid
15	L'enseignante de mathématique a écrit le problème sur le pistolet.	11	pistolet	86.6%	4.52	0%	100%	tableau
16	Ce matin le professeur a bu un robot.	8	robot	95.0%	4.79	0%	85.6%	café
17	Claude voit une annonce dans le fusil.	7	fusil	89.8%	4.63	0%	93.8%	journal
18	Suzanne mange un cornet de trésor.	6	trésor	84.8%	4.46	0%	94.8%	crème glacé, glace
19	Ils sont assis ensemble sans dire un seul poil.	9	poil	87.8%	4.61	0%	99.0%	mot
20	Le chaton joue avec la pelote de fenêtre.	8	fenêtre	84.7%	4.61	0%	96.9%	laine
21	Alice va à la bibliothèque pour emprunter un serpent.	9	serpent	85.8%	4.47	0%	96.9%	livre
22	Jean a pêché un gros casino.	6	casino	91.0%	4.71	0%	98.0%	poisson
23	Claire a envoyé la carte d'anniversaire par la colline.	10	colline	83.3%	4.46	0%	96.9%	poste

24	L'ambulance approche, j'entends la planète.	7	planète	93.0%	4.75	0%	94.8%	sirène
25	Papa a tranché la dinde avec un fauteuil.	8	fauteuil	90.9%	4.68	0%	100%	couteau
26	Elle coupe les légumes sur le cigare.	7	cigare	93.9%	4.70	0%	85.7%	comptoir
27	Ils ont pris le pont pour traverser la médaille.	9	médaille	91.9%	4.70	0%	90.7%	rivière
28	Les abeilles récoltent du pollen pour faire du crâne.	9	crâne	93.8%	4.77	0%	100%	miel
29	L'enseignant lui rappelle de faire son motel.	8	motel	89.9%	4.60	0%	84.5%	devoir
30	Ma tondeuse est brisée, je ne peux pas tondre le pantalon.	11	pantalon	87.8%	4.57	0%	96.9%	gazon
31	Annie a pris un mouchoir pour se moucher le bâton.	10	bâton	89.9%	4.68	0%	100%	nez
32	La professeure a aiguisé son camion.	6	camion	89.8%	4.67	0%	96.9%	crayon
33	Il a envoyé la lettre sans un fantôme.	8	fantôme	92.9%	4.66	0%	87.6%	timbre

34	Charles se brosse les cheveux avec la batterie.	8	batterie	91.0%	4.68	0%	100%	brosse
35	Ce garçon lit beaucoup de miel.	6	miel	95.0%	4.78	0%	86.6%	livres
36	Éloi allume sa pipe avec une peinture.	7	peinture	92.0%	4.68	0%	91.8%	allumette
37	Le chanteur a chanté une belle larme.	7	larme	85.7%	4.42	0%	86.6%	chanson
38	Le poète a écrit un canapé.	6	canapé	89.9%	4.65	0%	88.7%	poème
39	Pour protéger sa tête du soleil, Nicole porte un tigre.	10	tigre	93.8%	4.69	0%	99.0%	chapeau
40	Luc verse le jus dans un requin.	7	requin	87.9%	4.67	0%	95.9%	verre
	Average	**8.4**		**89.5%**	**4.62**	**0%**	**93.9%**	
	Maximum	**14**		**95.0%**	**4.79**	**0%**	**100.0%**	
	Minimum	**6**		**80.8%**	**4.35**	**0%**	**81.4%**	

	Sentences with a congruent word ending							
				Semantic Plausibility		Sentence Completion		
#	Sentence	Number of words	Target word	% of participants who answered 1-2	Average rating	Cloze probability for target	Cloze probability for other word produced	Other word produced
1	Le cellulaire est neuf, il est encore dans sa boîte.	10	boîte	92.8%	1.36	81.4%	Not applicable (N/A)	Not applicable (N/A)
2	Mon père a mis la vinaigrette dans la salade.	9	salade	88.8%	1.43	93.8%	N/A	N/A
3	Le Père Noël a bu le lait mais a laissé le biscuit.	12	biscuit	88.9%	1.38	90.7%	N/A	N/A
4	L'archer a tiré sa flèche.	6	flèche	93.8%	1.27	89.8%	N/A	N/A
5	Maude a fumé une autre cigarette.	6	cigarette	94.9%	1.16	93.8%	N/A	N/A

6	À l'école, l'enfant range son manteau dans son casier.	11	casier	94.9%	1.19	81.6%	N/A	N/A
7	Cette bague de fiançailles a un gros diamant.	8	diamant	90.9%	1.32	90.8%	N/A	N/A
8	Thomas fait réparer sa voiture au garage.	7	garage	97.0%	1.17	91.8%	N/A	N/A
9	Papa lit un article dans le journal.	7	journal	93.9%	1.23	95.9%	N/A	N/A
10	Pour l'Halloween, il a acheté un nouveau costume.	9	costume	95.0%	1.24	84.7%	N/A	N/A
11	Il ne peut pas chanter car il a mal à la gorge.	12	gorge	94.0%	1.30	81.4%	N/A	N/A
12	Laurent sèche ses mains avec la serviette.	7	serviette	88.9%	1.40	92.8%	N/A	N/A
13	Le lion est le roi de la jungle.	8	jungle	91.9%	1.29	89.8%	N/A	N/A
14	Nous allons manger au restaurant.	5	restaurant	93.8%	1.26	92.9%	N/A	N/A
15	Cette machine distributrice accepte seulement de la monnaie.	8	monnaie	94.9%	1.27	96.9%	N/A	N/A

16	Le patient prend de l'eau pour avaler la pilule.	10	pilule	93.0%	1.27	92.9%	N/A	N/A
17	Elle prend son café avec de la crème.	8	crème	94.9%	1.23	84.7%	N/A	N/A
18	La flèche a atteint la cible.	6	cible	94.9%	1.20	95.9%	N/A	N/A
19	Megan prend des photos avec sa nouvelle caméra.	8	caméra	95.9%	1.15	84.7%	N/A	N/A
20	Il tient son pantalon avec une ceinture.	7	ceinture	86.8%	1.45	79.6%	N/A	N/A
21	Iris a glissé sur la glace.	6	glace	94.9%	1.19	81.6%	N/A	N/A
22	Elles ont choisi d'aller voir une pièce de théâtre.	10	théâtre	95.9%	1.18	99.0%	N/A	N/A
23	Karine regarde l'heure sur sa montre.	7	montre	96.0%	1.14	100%	N/A	N/A
24	Il a tondu la laine du mouton.	7	mouton	96.0%	1.21	96.9%	N/A	N/A
25	Annette se bronze au soleil	5	soleil	92.8%	1.27	90.8%	N/A	N/A
26	Simon mesure chaque ligne avec une règle.	7	règle	96.9%	1.15	99.0%	N/A	N/A
27	Le bébé voit son reflet dans le miroir.	8	miroir	93.9%	1.26	96.9%	N/A	N/A

28	J'ai mis la nappe sur la table.	8	table	96.9%	1.13	97.9%	N/A	N/A
29	Mon voisin a mis une fontaine dans son jardin.	9	jardin	93.8%	1.26	85.6%	N/A	N/A
30	Diana saupoudre les biscuits de sucre.	6	sucre	94.8%	1.22	82.6%	N/A	N/A
31	Ce boucher vend beaucoup de viande.	6	viande	97.0%	1.13	92.8%	N/A	N/A
32	La fille a jeté les déchets dans la poubelle.	9	poubelle	96.9%	1.12	96.9%	N/A	N/A
33	Paul aime le pepperoni sur sa pizza.	7	pizza	96.9%	1.12	98.0%	N/A	N/A
34	Mon frère a acheté un chandail au magasin.	8	magasin	97.0%	1.13	83.7%	N/A	N/A
35	Autour du cou, elle porte un collier.	7	collier	94.9%	1.18	84.5%	N/A	N/A
36	L'instrument du pianiste est le piano.	6	piano	96.0%	1.17	100%	N/A	N/A
37	Le randonneur a réussi à atteindre le plus haut sommet.	10	sommet	88.8%	1.37	89.8%	N/A	N/A
38	Léo écrit une lettre sur la feuille de papier.	9	papier	95.9%	1.17	84.5%	N/A	N/A

39	L'alpiniste a atteint le sommet de la montagne.	9	montagne	95.9%	1.15	95.9%	N/A	N/A
40	Il y a beaucoup de coquillages sur cette plage.	9	plage	96.9%	1.12	97.9%	N/A	N/A
	Average	**7.9**		**94.2%**	**1.23**	**91.0%**		
	Maximum	**12**		**97.0%**	**1.45**	**100%**		
	Minimum	**5**		**86.8%**	**1.12**	**80%**		

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