Age- and gender-related differences in verbal semantic processing: the development of normative electrophysiological data in the Flemish population

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Abstract: Categorical and associative relationships among words are two key forms of semantic knowledge. In this study, we examined ageing and gender effects on the processing of both types of semantic relationships by using the event-related potential technique. Moreover, we aimed to develop normative electrophysiological data for clinical purposes. One hundred and ten healthy subjects were divided among three age groups and subjected to two auditory word priming paradigms. Early auditory processing was influenced by increasing age as shown by larger P1 amplitudes and by the delayed onsets of the N1 and P2. Conversely, ageing effects on the main N400 effect were limited to an increased right hemispheric lateralisation pattern for associative relationships. Gender effects could be demonstrated with women showing larger P2 amplitudes and larger semantic priming effects in comparison to men. The interpretation of these findings is discussed and the practical utility of the obtained normative data is emphasized.

Keywords: ageing; gender; semantics; event-related potentials

1. Introduction

Language comprehension is a central aspect in human life and mainly depends on the semantic (or conceptual) knowledge that is acquired over a lifetime (Kutas & Federmeier, 2000). More precisely, verbal and nonverbal experiences expose individuals to multimodal features (e.g. visual, auditory, motor and tactile properties), that are encoded, integrated and stored in our brain (semantic memory). In order to retrieve and to select the information that is context-relevant, a top-down/executive manipulation of semantic knowledge (semantic control) is required, as highlighted in the controlled semantic cognition framework (Ralph et al., 2017). Two important relationships in semantic memory are categorical and associative ones (Caramazza & Mahon, 2003; Estes et al., 2011; Lin & Murphy, 2001; Mahon & Caramazza, 2009; Mirman et al., 2017). Categorical relationships refer to concepts that share overlapping features, independent of time and space. Usually, categories are hierarchically represented based on their specificity level (e.g. animal – dog – poodle) (Murphy & Lassaline, 1997). Associative relationships apply to concepts that evoke thoughts of one another. Classically, associations are derived from free-word association tasks during which participants are instructed to produce the first word that comes to mind in response to a certain cue word. The probability (%) of producing a target word in response to this cue word is their association strength (Nelson et al., 2000). Associated words are always characterized by a more specific relation, which can be semantic in nature, e.g. synonymy (beautiful - pretty), antonymy (black-white), hyponymy (flower - tulip), hyperonymy (horse - animal), co-hyponymy (dog-cat), an entity-based relation (apple – green)or a thematic relation[1] (Estes et al., 2011; De Deyne & Storms, 2008). In comparison to associative links, categorical relationships are cognitively more demanding as they are more distant and abstract in nature (Kotz et al., 2002; Sachs et al.,

[1] Thematic relations refer to concepts that perform complementary roles in an event and are often spatial (lawyer – court), temporal (summer – holiday), causal (to fall – pain), functional (bucket – to clean), possessive (butcher - knife) or productive (cow - milk) in nature (Estes et al., 2011; Lin & Murphy, 2001; Mirman et al., 2017).

2008a). As a result, the latter relationships are developed to more sophisticated levels later on in childhood (Whitney & Kunen, 1983) and deteriorate first in the context of semantic dementia (Moss et al., 1995; Tyler & Moss, 1998; Nakamura et al., 2000). At the neural level, categorical and associative relationships engage the same core semantic network, including the bilateral anterior temporal lobes, the superior temporal sulci, the left ventral prefrontal cortex (PFC) and the posterior middle temporal cortices (Jackson et al., 2015). Although it has been suggested that the anterior temporal lobes are particularly important for categorical relationships and the parieto-temporal cortices for the associative ones, this should be affirmed by future research (for a systematic review see Mirman et al., 2017). Finally, a larger allocation of cognitive resources during the processing of categorical processing results in a more pronounced activation of the PFC (Jackson et al., 2015) and more reliance upon right hemispheric areas (Kotz et al., 2002; Sachs et al., 2008b; Sass et al., 2009). Inevitably, semantic neural networks are subject to structural changes with increasing age. Typically, the grey matter volume of the lateral and orbital prefrontal cortex (Tisserand et al., 2002; Raz et al., 2004) and the integrity of frontal white matter (Bennett et al., 2010; Burzynska et al., 2010; Head et al., 2004; Madden et al., 2012; Salat et al., 2005) are reduced to the greatest extent in older adults. These structural alterations are associated with decrements of multiple executive functions (e.g. inhibitory control, shifting, updating, etc.) that can affect semantic control in particular (Davis et al., 2009; Gunning-Dixon & Raz, 2003; Kennedy & Raz, 2009; Manard et al., 2016). In addition to age-related structural changes, anatomical differences between the linguistic cortices of men and women have been described. For example, larger superior temporal volumes have been observed in females (Good et al., 2001; Sowell et al., 2007) from childhood until advanced age (Sowell et al., 2007). As such, whether and how healthy ageing and gender influence aspects of (verbal) semantic processing are intriguing research topics.

In scientific research, word priming tasks are commonly used to investigate the integrity and retrieval of semantic knowledge. At the behavioural level, these tasks reveal faster and more accurate responses during lexical decision or pronunciation tasks when a (target) word is preceded by a semantically related (prime) word than by an unrelated (prime) word (Laver & Burke, 1993; Meyer & Schvaneveldt, 1971; Neely, 1991). This processing benefit is referred to as the "semantic priming effect" and can occur due to an association among words (e.g. cow-milk) and/or (pure) feature overlap (e.g. cat-dog/bike-car) (Lucas, 2000; McNamara, 2005). The latter effects have been explained by automatic (implicit) spreading activation as well as by two controlled, attention-demanding (explicit) mechanisms, largely depending on the nature of the experimental task (e.g. the stimulus onset asynchrony, SOA) (Table 1). In the majority of healthy ageing studies, older individuals show equivalent semantic priming effects as the young subjects, both when automatic or controlled processes are targeted (Burke & White, 1987; Chiarello et al., 1985; Howard, 1983; Madden, 1986; Ober et al., 1991) and independent of whether categorical or associative relationships are primed (Giffard et al., 2003). The latter results support the general view that the integrity of semantic memory is relatively resistant to ageing effects (Park et al., 2002) and, hence, that connections between semantic memory nodes remain relatively intact in older adulthood (Federmeier et al., 2002). A decline of general cognitive functions including decrements in processing speed (Park et al., 2002; Salthouse, 1996), inhibitory control (Hasher & Zacks, 1988; Lustig et al., 2007) and working memory (Park et al., 2002; Wingfield et al., 1988) can, however, influence semantic retrieval (and selection) in older adults (Hoffman, 2018; Meyer & Federmeier, 2010). In this context, the less frequently observed "hyperpriming" effect (Laver & Burke, 1993) has been linked to general cognitive slowing in normal aging (Giffard et al., 2003; Myerson et al., 1992; Myerson et al., 1997). Moreover, an age-related increase in the minimum SOA at which semantic priming occurs has been described (Howard et al., 1986). Remarkably, the efficient use of categorical and associative relationships seems to be affected by age in a different way. In more detail, word list recall performance is more variable for categorically linked items than for associatively linked words (Belacchi & Artuso, 2018) with a less pronounced benefit from categorical relationships beyond the age of 65 years (Amhrein et al., 1998; Belacchi & Artuso, 2018; Taconnat et al., 2009). Thus, the most cognitively demanding type of relationships (categorical) seems to be the most prone to age-related declines (Belacchi & Artuso, 2018). Finally, to the best of our knowledge, no previous behavioural studies investigated gender-related effects on semantic priming or on the use of categorical versus associative relationships. Nonetheless, women often outperform men on verbal learning and memory tasks, independent of their age (Herlitz & Rehnman, 2008; Kimura, 2002; Maitland et al., 2004; McCarrey et al., 2016; Munro et al., 2012).

Behavioural experiments do, however, not allow an online monitoring of the sensory and cognitive (sub)processes underlying semantic behaviour. Understanding an auditorily presented word, for example, requires a successful completion of multiple (sub)stages, i.e. acoustic processing, phonological discrimination, lexico-semantic access, the processing of semantic relations and context integration within milliseconds of time (Friederici, 2002). Whether and which stages in the processing stream are influenced by normal aging and/or by gender can only be properly investigated by means of a technique with excellent temporal resolution. A good method of choice is the event-related potential (ERP) technique, providing "a continuous, millisecond-by-millisecond measure of processing, beginning prior to the stimulus and extending past the response" (Luck, 2014, page 25). During a semantic (word) priming task in the auditory modality, multiple responses are elicited in normal-hearing healthy adults, including the sensory (exogenous) P1, N1, and P2, and the cognitive (endogenous) N400 (Giaquinto et al., 2007; Hagoort et al., 1996; Räling et al., 2015; Räling et al., 2016). Each potential is characterised by its amplitude, or the strength of the response in microvolt (μV), its latency, or the timing in milliseconds (ms), and its topography, or the distribution of the electrical activity among the scalp (Luck, 2014). The P1, N1 and P2, peaking around 50, 100 and 200 ms after stimulus onset respectively, have been associated with the early cortical processing stages of auditory stimuli, including auditory detection. The P1-N1-P2 complex comprises obligatory responses that are elicited by wide ranges of acoustic stimuli and that are independent of the attentional mode of the listener (Alain & Tremblay, 2007). However, attended stimuli do elicit larger amplitudes in the N1-P2 latency range (Hillyard et al., 1973; Woldorff et al., 1993). Intact auditory word processing implies that (often overlapping) P1-N1-P2 responses are recorded in response to the time-varying acoustic changes within a word (i.e. the acoustic change complex/ACC, Martin et al., 2008). When elicited, the ACC reflects intact cortical access to the acoustic features of speech (Kaukoranta & Lounasmaa, 1987; Martin et al., 2008; Ostroff et al., 1998), which is necessary for advanced word processing levels. Within this context, multiple studies found phonological, lexical and semantic effects in the latency range of the P2 and even ahead of it (for a review see Pulvermüller et al., 2009). The N400 component, initially discovered by Kutas and Hillyard (Kutas & Hillyard, 1980), is described to peak around 400 ms after stimulus onset, although a broadly distributed plateau without a clear peak is often observed (Bridger et al., 2012; Daltrozzo et al., 2007; Giaquinto et al., 2007). The N400 is the most-studied language related ERP-component and is typically largest over centro-parietal scalp regions (Kutas & Federmeier, 2011). In general, the N400 is elicited by a wide variety of (potentially) meaningful stimuli that are not restricted to the auditory domain (Federmeier & Laszlo, 2009; Kutas & Federmeier, 2000, 2011), and exhibits higher amplitudes during focused attention than during passive tasks (Erlbeck et al., 2014). Although its exact processing nature remains a topic of debate (Kutas & Federmeier, 2011; Lau et al., 2008; Van Petten & Luka, 2012), the N400 is considered to be “a neural marker of active processing in semantic memory” (Federmeier & Laszlo, 2009). ERP word priming studies support this view as the amplitude of the N400 is modulated by the semantic (categorical or associative) relationship with a preceding context, i.e. smaller amplitudes to "bike" (target) than to "tree" (target) if preceded by "car" (prime). The difference between the ERPs elicited by semantically unrelated and related targets is described as the "N400 priming effect" (Holcomb & Neville, 1990; Koivisto & Revonsuo, 2001). The latter effect corresponds to the (aforementioned) behavioural priming results and, hence, can be explained by automatic spreading activation and/or by controlled mechanisms (Table 1).

Healthy aging effects on the acoustic (P1-N2-P2) change complex elicited by (attended) words have been investigated to a limited extent only. To the best of our knowledge, no results on the P1 are available. Regarding the N1, elderly subjects have shown equivalent N1 amplitudes (Federmeier et al., 2003; Giaquinto et al., 2007; Woodward et al., 1993) and similar (Giaquinto et al., 2007; Woodward et al., 1993) or increased N1 latencies (Federmeier et al., 2003) in comparison to young individuals. For the P2 component, equivalent amplitudes and significantly longer latencies have been reported in elderly compared to young subjects (Federmeier et al., 2003; Giaquinto et al., 2007; Woodward et al., 1993). Similarly, research towards ageing effects on the amplitude, latency and topographical distribution of the N400 word priming effect is very limited in the auditory modality[2]. During a category-member verification task, Räling et al. (2016) reported on absent N400 effects at centro-parietal electrode positions in older individuals (mean age: 66.7 years, range: 49-79 years). These findings were linked to the IDH of Hasher and Zacks (1988). The IDH states that healthy aging is accompanied by a decreasing ability to inhibit the processing of irrelevant (perceptual or cognitive) information. As such, insufficient inhibition of the unrelated targets could explain

[2] In the visual modality, Grieder et al. (2012) found intact N400 effects during a word priming task with a short SOA. Diminished N400 effects have been revealed in case of long SOAs (Bornkessel-Schlesewsky et al., 2015; Cameli, 1999; Federmeier et al., 2010; Gunter et al., 1998; Iragui et al., 1996; Kutas & Iragui, 1998; Miyamoto et al., 1998).

reduced amplitudes of the N400 effect. Finally, the authors observed a topographical shift from a bilateral centro-parietal N400 effect in the young towards a right frontal effect in the elderly, which corresponds well to the HAROLD (hemispheric asymmetry reduction in older adults, Cabeza, 2002) and PASA (posterior-to-anterior shift in ageing; Davis et al., 2008) models which are based on spatial imaging results. In contrast to the findings of Räling et al. (2016), the size of the associative N400 effect was not significantly affected in elderly participants (mean age: 72 years, range 57-79 years) who were instructed to listen to natural speech (contrast: anomalous associated versus anomalous unassociated sentences, Federmeier et al., 2003). Moreover, no age-related differences were detected regarding the topographical distribution (Federmeier et al., 2003). In both studies, effects of healthy ageing on the latency of the N400 effect were not considered. Altogether, the categorical N400 effect seems to be the most prone to healthy ageing effects, but this needs further confirmation.

Electrophysiological research towards gender differences in auditory semantic priming is scarce as well. In a previous study, Daltrozzo et al. (2007) found earlier and larger associative N400 effects in women (mean age: 43.1 years, SE: 6.3 years) than in men (mean age: 40.7 years, SE: 5.6 years) at fronto-parietal and frontal electrodes respectively, although the amplitude differences reached only marginal significance after a Bonferroni-correction.

In the current study, we aimed to accomplish three main objectives. First of all, healthy ageing effects on the processing of both categorical and associative relationships are investigated by means of the ERP-technique. More precisely, the effects of increasing age on the amplitude, latency and topographical distribution of the N400 priming effect are examined, and the integrity of the early auditory complex (P1-N1-P2) is analysed. Multiple age groups (young, middle-aged and elderly) are included in order to represent a firm part of the ageing trajectory (Finch, 1991; Hedden & Gabrieli, 2004; Raz, 2009). Our second aim is to investigate the influence of gender on the processing of categorical and associative relationships and whether (possible) ageing effects are disclosed differently in male and female individuals. Finally, the third aim is to provide normative electrophysiological data for men and women of the three age groups (young, middle-aged and elderly). The latter normative data for semantic priming are intended to be useful for clinical purposes in Flemish patients with acquired language disorders (Cocquyt et al., 2020a), which has previously been demonstrated for phonological input processing (Aerts, Batens, et al., 2015; Aerts et al., 2013; Aerts, van Mierlo, et al., 2015a, 2015b; Cocquyt et al., 2020b).

Table 1: Overview of the three mechanisms explaining semantic priming effects (Neely, 1991).

Theory	**Interpretation**	**Task characteristics ***
Automatic spreading activation theory	"Processing a prime word automatically results in a spread of activation through the semantic network to the nodes that are semantically related to the prime word" (Laver & Burke, 1993, page 34). In case a prime word is followed by a semantically related target word, the latter word requires less sensory decoding and will be processed more efficiently.	SOA < 400 ms
Controlled prelexical prediction	Generation of target words that are semantically related to the preceding prime and, thus, expected within the context. Processing benefits will occur whenever the presented target corresponds to an expectation.	SOA > 400 ms
Controlled postlexical integration	Initiates after the target word is processed and verifies if the specific target fits well within the preceding context.	SOA > 400 ms

Note: SOA = stimulus onset asynchrony (the amount of time between the start of the prime word and the start of the target word); * based upon experiments in the visual modality, the SOA in auditory experiments depends on the duration of the words and on the presentation mode (monaural versus binaural stimulation)

2. Methods

2.1 Participants

One hundred and ten native Dutch-speaking volunteers[3], 55 men and 55 women, were included in this study. All participants were right-handed, as assessed by the Dutch Handedness Inventory (Van Strien, 1992), reported normal hearing and had no history of developmental speech/language disabilities or chronic neurological/neuropsychiatric disorders. In all subjects, the Dutch version of the Montréal Cognitive Assessment (MoCA; Nasreddine et al., 2004) was administered to exclude the presence of mild cognitive impairments (cut off score = 26). In order to investigate ageing effects, the participants were clustered in three different age groups namely the young (20-39 years), middle-aged (40-59 years) and elderly (≥ 60 years: 60-84 years). The young and middle-aged group each consisted of twenty men and twenty women, whereas the elderly group consisted of 15 men and 15 women. A description of the three age groups in terms of age, education level and MoCA scores can be found in Table 2. This study was approved by the Ethical Committee of the University Hospital Ghent and all the subjects signed an informed consent.

[3] In total, one hundred and twenty-five volunteers participated. Throughout the participant recruitment period, 15 individuals were excluded for the following reasons: technical issues (n=2), MoCA score < 26 (n=2), pronounced hearing loss (n=2), headache (n=1), tiredness (n=3), drop-out (n=1) and ambidexterity (n=4).

Table 2: Demographic details of the 55 male and 55 female participants, presented per age group.

	Young (20-39 years) Mean (SD)		Middle-aged (40-59 years) Mean (SD)		Elderly (60+ years) Mean (SD)	
	Male	Female	Male	Female	Male	Female
Age (years)	30.0 (5.8)	29.2 (5.6)	49.7 (4.4)	50.1 (6.2)	67.4 (7.4)	66.9 (6.0)
Education level [a]	3.5 (0.7)	3.4 (0.8)	3.4 (0.9)	2.9 (0.9)	2.9 (1.0)	2.4 (0.7)
MoCA score (/30)	28.3 (1.4)	28.6 (1.3)	28.4 (1.4)	29.0 (1.0)	27.3 (1.0)	27.2 (1.5)

Note: SD= standard deviation; MoCA = Montréal Cognitive Assessment (Nasreddine et al., 2004)

[a] The level of education was rated on a 5-point scale: 1, Primary school; 2, Secondary school; 3, Bachelor; 4, Master; 5, PhD (based on Guillem & Mograss, 2005).

2.2 Behavioural evaluation

Standardised measures of semantic processing abilities were obtained by means of two subtests of the Dutch Semantic Association Test (SAT), namely verbal semantic association and oral naming (Visch-Brink et al., 2005). Total subtest scores of ≤ 25 are indicative of verbal semantic and oral naming disorders in the context of aphasia. Unfortunately, a standardised test for the comprehension of categorical relationships among words is not available for the Dutch language. However, the behavioural accuracies (correct button press responses) for both the categorical and the associative priming task during electroencephalographic (EEG) recording were collected.

2.3 Electrophysiological recording

2.3.1 Stimuli, procedure and EEG recording parameters

Stimuli - During EEG recording, a categorical and an associative priming task were used, each consisting of 120 auditorily presented Dutch word pairs (first word = prime, second word = target). In both experiments, half of the word pairs (n=60) were related in meaning and the other half were unrelated. The tasks were adapted from Hagoort et al. (1996).

In the categorical priming task, all stimuli were prototypical members of several semantic categories (Noordman-Vonk, 1977). The material was not characterised by a dominant category (e.g. “tools” or “plants”) in order to avoid category-specific processing advantages for males or females (Barbarotto et al., 2002; Bermeitinger et al., 2008; Capitani et al., 1999). Primes and targets were either members of the same (related condition) or different categories (unrelated condition), but none of the word pairs were characterised by an associative relation[4]. In the associative priming task, word pairs were either strongly associated (related condition, mean association frequency: 45.9%, SD 15.6), or not associated at all (unrelated condition), based upon available Dutch word association norms (de Groot, 1980; de Groot & De Bil, 1987; Lauteslager et al., 1986). In the related trials, the associated words were characterized by the following semantic relations: synonymy (n=18), antonymy (n=13), hyponymy (n=1), hyperonymy (n=1), co-hyponymy (n=2), an entity-based relation (n=6)and a thematic relation[5] (n=19). All the words were spoken with a flat intonation by a male native speaker of Dutch and were recorded using a Rode NT1-a microphone. The stimulus material of the categorical and associative priming task can be found in Appendix 1 and 2 respectively.

In both priming tasks, the target words were the focus of our analyses and were therefore matched on psycholinguistic characteristics that were not of interest for further analyses. There were no significant differences across the related and unrelated conditions in the mean values of word frequency (SUBTLEX-NL - Keuleers et al., 2010), phonological length, the amount of phonological neighbours (CLEARPOND Dutch – Marian et al., 2012), concreteness (Brysbaert et al., 2014), imageability (van Loon-Vervoorn, 1985), age of acquisition, valence, arousal, dominance (Moors et al., 2013) and total duration. Table 3 provides a summary of all the

[4] In the original study of Hagoort et al. (1996), twenty subjects had to write down the first three words that came to mind for every prime word. One or more occurrences of the target word among the responses to a prime, led to the removal of this word pair from the stimulus list. In this way, it was established that none of the categorically related words were also associatively related.

[5] Spatial (n=2), causal (n=5), functional (n=11) and possessive (n=1)

psycholinguistic characteristics. There were no Dutch norms for familiarity that would include all (or most of) the stimuli used in this study. However, familiarity is significantly correlated with multiple other variables that we were able to account for (i.e. word frequency, imageability, concreteness, valence and arousal) (Citron et al., 2014; Stadthagen-Gonzalez & Davis, 2006).

Table 3: Psycholinguistic characteristics (mean – standard deviation) of the related and unrelated target stimuli in the categorical and associative priming task.

	Categorical priming		Associative priming	
	Related	Unrelated	Related	Unrelated
Stimulus duration (ms)	581 (118)	582 (126)	510 (100)	511 (111)
Phonological length	4.7 (1.6)	4.6 (1.4)	4.2 (1.2)	4.1 (0.9)
SUBTLEX-NL frequency*	38.4 (59.7)	33.2 (56.1)	70.2 (81.3)	70.8 (95.0)
PTAN	7.9 (8.8)	7.2 (7.7)	13.3 (8.6)	11.5 (8.1)
Concreteness	4.4 (0.6)	4.5 (0.6)	3.6 (1.1)	3.7 (1.1)
Imageability	6.3 (0.6)	6.3 (0.5)	5.7 (1.0)	5.8 (1.0)
Age of acquisition	5.2 (1.4)	5.7 (1.6)	5.0 (1.1)	5.3 (1.3)
Valence	4.2 (0.6)	4.2 (0.7)	4.2 (1.0)	4.4 (1.1)
Arousal	3.9 (0.8)	3.8 (0.7)	4.0 (0.9)	4.0 (0.9)
Dominance	4.1 (0.5)	4.0 (0.5)	4.2 (0.7)	4.2 (0.6)

Note: * frequency per million words; PTAN = total amount of phonological neighbours

Procedure – The participants were comfortably seated at a distance of approximately 70 cm from a Dell-laptop screen. In order to elicit maximal N400 responses, we preferred using focused (active) tasks (Erlbeck et al., 2014), instead of the passive modus applied in the original experiments of Hagoort et al. (1996). The instruction was to listen to the prime-target pairs and to judge the semantic relationship between both words, by means of a button press response. All the stimuli were presented binaurally with ER1-insert earphones at a comfortable listening level. For the categorical priming experiment, the inter-stimulus interval (ISI) varied between 830 and 1520 ms, and for the associative task, the range of the ISI was 860-1550 ms. In both experiments, a long SOA (1800 ms) was chosen to ensure that prime words were entirely processed before the onset of a target word (see also Kojima & Kaga, 2003). In this way, large N400 effects were expected (Anderson & Holcomb, 1995). The inter-trial interval (ITI) was 2500 ms.

The at random presentation of word pairs was accomplished by means of the E-Prime 3 Presentation software (Psychology Software Tools, Pittsburgh, PA). In E-Prime 3, the accuracies and button press reaction times (ms) were registered. During all trials, participants had to focus on a white fixation cross, centred on a black screen, in order to reduce vertical and horizontal eye movements. Minimum one second after the presentation of a target word, subjects had to press their left or right index finger on the green or red button for related and unrelated pairs respectively. The button press response was delayed in order to avoid contamination of the N400 with response-related potentials (van Vliet et al., 2014). The allocation of buttons was changed for half of the male and half of the female participants in each age group. A schematic overview of the task procedure is provided in Figure 1.

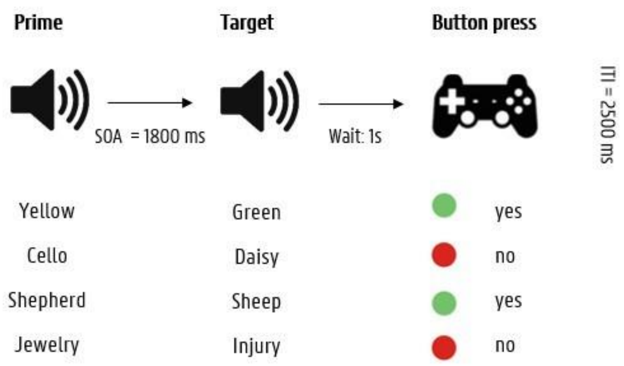


Figure 1: Schematic overview of the task procedure. Examples of the prime and target stimuli are presented for the categorically related, (categorically) unrelated, associatively related and (associatively) unrelated condition respectively (SOA = stimulus onset asynchrony, ITI = intertrial interval, ms = milliseconds, s = second).

The two experiments consisted of 7 blocks each with short pauses in between. For both the categorical and the associative priming task, a practice block preceded the experimental blocks in order to familiarize the subjects with the test procedure and to assure that the stimulus intensity was sufficient for an accurate intelligibility of the prime and target words. All participants were tested by the same researcher (E.M.C., first author) to ensure that everyone received identical instructions. The total duration of the experiment lasted about two hours.

EEG recording parameters – In view of the clinical purposes, the EEG was recorded from 32 Ag/AgCl electrodes buttoned directly into an elastic cap (Braincap, Brain Products, Germany), including the following scalp sites: Fp1/2, Fpz, F3/4, F7/8, Fz, FC1/2, FC5/6, C3/4, T7/8, Cz, CP1/2, CP5/6, P3/4, P7/8, Pz, TP9/10, POz, O1/2 and Oz (following the International 10-20 system, American Electroencephalographic Society, 1991). AFz and FCz were used as the ground and the online reference electrode respectively. The electrode impedances were kept below 10 kΩ by using an abrasive electrolyte gel (Abralyt 2000, Easycap). The EEG signal was processed through an actiCHamp amplifier (BrainAmp DC/MR plus) and was digitised with a sampling rate of 500 Hz (BrainVision Recorder, Software version 1.20.0802, Brain Products GmbH, Gilching, Germany).

2.3.2 EEG analysis and data-extraction

The offline EEG analysis was performed separately for the categorical and the associative priming task, using BrainVision Analyzer 2.1 (Brain Products, Germany). Firstly, the continuous EEG-data were band-pass filtered between 0.3 and 30 Hz (half-amplitude cut-off, 12 dB/octave roll-off) and notch-filtered at 50 Hz. Independent Component Analysis (ICA) was used in order to remove the artefacts induced by eye blinks and horizontal eye movements. The identification and removal of the artefact-related components was based upon visual inspection of the waveforms and their topographical scalp distribution (Jung et al., 2000). The ICA-corrected data were then re-referenced to the algebraic average of the left and right mastoids (Duncan et al., 2009). Only trials with correct behavioural responses were included for further analysis. For the related and unrelated trials separately, a segmentation was performed into 1200 ms long epochs, starting from 200 ms prior to the onset of the target word and continuing for 1000 ms post-onset. A baseline correction from 200 ms to 0 ms prior to the onset of the target words was applied on all the segments. Thereafter, automatic artefact-rejection was applied by using the following rejection criteria: 1) a maximum gradient criterion of 75 µV, 2) a minimal/maximal amplitude criterion of 75 µV, 3) a maximum difference criterion of 200 µV and 4) a low activity criterion of 0.5 µV during 100 ms. Participants were excluded if more than 25% of the trials were rejected (Mini ERP Bootcamp, Birmingham, Kappenman and Luck, 2018). Table 4 provides an overview of the amount of included trials in both priming experiments for men and women of each age group. Finally, the artefact-free data-segments were separately averaged for the related and unrelated targets.

Table 4: Overview of the amount of included trials (mean – standard deviation) in the female and male subjects of each age group for the categorical and associative priming experiment.

	Categorical priming				Associative priming			
	Male		Female		Male		Female	
Age group	Related	Unrelated	Related	Unrelated	Related	Unrelated	Related	Unrelated
Young	55 (4)	56 (4)	55 (3)	56 (3)	57(3)	57 (3)	57 (2)	58 (2)
Middle-aged	55 (3)	57 (3)	56 (4)	56 (3)	58 (2)	58 (2)	58 (3)	57 (3)
Elderly	54 (5)	55 (4)	54 (3)	56 (2)	55 (4)	56 (4)	57 (3)	56 (4)

The extraction of amplitude and latency values occurred in component-specific measurement windows. For both the related and unrelated conditions, amplitudes of the sensory P1, N1 and P2 were measured as the mean voltage between 60-100 ms, 100-180 ms and 180-300 ms respectively, at frontal (F3, Fz, F4) and at central (C3, Cz, C4) electrode sites (Aerts et al., 2013; Giaquinto et al., 2007). For the N400, parietal electrode sites (P3, Pz, P4) were added (Daltrozzo et al., 2007; Erlbeck et al., 2014; Erlbeck et al., 2017; Ford et al., 1996; Kawohl et al., 2010) and the amplitudes were measured as the mean voltage between 300-800 ms (Räling et al., 2015; Räling et al., 2016; Revonsuo et al., 1998). The onset latency of the sensory components (N1 and P2) was quantified as the 50% fractional peak latency (Kiesel et al., 2008), namely the point in time at which the average amplitude reaches 50% of its maximum (peak) value (Luck, 2014). The latencies were extracted at the central (N1) or at the frontal (P2) electrodes of which the averages were calculated. For the P1, the onset latencies were not calculated due to an unreliable peak detection, and this especially in the young group. Fractional (20%) area latencies were used to determine the onset of the N400 (Newman et al., 2012; Willems et al., 2008) at the central electrode positions (Aerts et al., 2013; Giaquinto et al., 2007).

The majority of our analyses targeted the N400 priming effect and, thus, most measures were taken in the difference waves, computed by the subtraction of the averaged ERPs to related words from the averaged ERPs to unrelated words. In order to evaluate the time course of the N400 effects, mean amplitudes were measured across the broad time of 300-800 ms and across five windows of 100 ms each, namely 300-400 ms, 400-500 ms, 500-600 ms, 600-700 ms and 700-800 ms (see Iragui et al., 1996; Räling et al., 2015; Räling et al., 2016 for similar analyses) at the aforementioned frontal, central and parietal electrode positions. Finally, the onset of the N400 effect was estimated by calculating fractional area latencies, more specifically, the latencies at which the mean negative amplitude of the difference wave between 300-800 ms reached 20% of its total value (Newman et al., 2012; Willems et al., 2008). The extraction of latencies was restricted to the central electrodes (C3, Cz and C4) of which the average was calculated.

2.4 Statistical analyses

The statistical analyses were performed in IBM SPSS Statistics 25 and the .05 alpha error level was used to determine statistical significance. The accuracy data for the behavioural and electrophysiological tasks were subjected to univariate analyses of variance (ANOVA) with age group (young, middle-age or elderly) and gender (male or female) as independent variables. The reaction time data for the electrophysiological experiments were not analysed due to the fact that a delayed response task was used. For the analysis of the electrophysiological measures, mean amplitudes were analysed by means of a repeated-measures ANOVA with age group and gender as between-subject factors and condition (related or unrelated) and anterior-to-posterior (A-P) distribution (frontal, central and/or parietal) as within-subject factors. For the P1, N1 and P2 components, the left, midline and right electrode sites were collapsed as anterior to central sites, whereas for the N400 components and the N400 effects (difference waves), measures were collapsed among the 9 topographical sites (F3, Fz, F4, C3, Cz, C4, P3, Pz and P4). Furthermore, the factor condition was not of relevance during the statistical analysis of the N400 effect, but the within-subject factor time-window was used in order to investigate possible timing-related differences between age groups and/or genders. Finally, ageing and gender effects on the main N400 effect (between 300-800 ms) were investigated by means of univariate analyses of variance. Separate repeated-measures ANOVA were used in order to examine possible effects of age group and gender on the onset latencies of the N1, P2 and N400 since the latter values were extracted in and compared between the related and the unrelated condition. Conversely, ageing and gender effects on the onset of the N400 effects were investigated by means of univariate analyses of variance. Regarding the topographical distribution of the N400 effect between 300-800 ms, a repeated-measures ANOVA with age group and gender as between-subject factors and A-P distribution (frontal, central or parietal) and lateralisation (left hemisphere, midline, right hemisphere) as within-subject factors was used. In order to compensate for inhomogeneous covariances, the Greenhouse-Geisser correction was applied whenever there were more than two levels of a within-subject factor (Luck, 2014, page 320). If appropriate, the adjusted F-values, p-values and degrees of freedom were reported. Post hoc comparisons were conducted using the Bonferroni procedure.

Lastly, Spearman correlation coefficients were calculated between the size and the onset of the categorical and associative N400 effect on the one hand, and the corresponding behavioural accuracies (online button press responses) on the other hand (Aerts et al., 2013; Kojima & Kaga, 2003).

3. Results

3.1 Behavioural accuracy

The standardised semantic evaluation, consisting of the SAT subtests "verbal association" and "oral naming", revealed a high accuracy in the three age groups (Table 5). However, for the verbal association scores, a univariate analysis of variance (ANOVA) showed a significant main effect of age group ($F(2, 104) = 6.87$, $p<0.01$). Post hoc comparisons revealed significant lower verbal association scores for the elderly in comparison to both the young and the middle-aged individuals (mean differences: 0.8, 95% CI [0.2 – 1.3], $p<0.01$). Conversely, the oral naming scores were not significantly different between the three age groups. Moreover, there were no significant differences between the behavioural performanceof male and female subjects on both SAT subtests, as well as no significant interaction effects between gender and age group.

The behavioural accuracy on the semantic tasks during EEG recording significantly differed between the three age groups, although for the categorical priming experiment only ($F(2, 104) = 6.41$, $p<0.01$). Similar to the standardised evaluation results, post hoc comparisons revealed no significant differences between the scores of the young and the middle-aged, but the elderly had significantly lower scores (mean difference elderly - young: 1.8, 95% CI: [0.5 – 3.2], $p<0.01$; mean difference elderly – middle-age: 1.6, 95% CI [0.3 – 3.0], $p<0.05$). Finally, no gender-related performance differences were detected in the three age groups.

Table 5: Overview of the behavioural accuracy results (mean – standard error) for the male and female subjects of each age group.

	Young (20-39 years)		Middle-aged (40-59 years)		Elderly (60+ years)	
	Male	Female	Male	Female	Male	Female
SAT: verbal association (/30)	29.3 (0.3)	29.2 (0.2)	29.3 (0.2)	29.2 (0.2)	28.5 (0.3)	28.4 (0.2)
SAT: oral naming (/30)	29.5 (0.1)	29.5 (0.2)	29.5 (0.2)	29.5 (0.2)	29.2 (0.3)	29.5 (0.2)
Categorical priming (/120)	116.1 (0.4)	116.3 (0.6)	115.8 (0.4)	116.1 (0.5)	114.3 (0.7)	114.3 (0.7)
Associative priming (/120)	117.8 (0.3)	117.9 (0.3)	118.0 (0.3)	118.1 (0.4)	117.3 (0.5)	116.9 (0.9)

* Note: SAT = Semantic Association Test (Visch-Brink et al., 2005)

3.2 Event-related potentials

In the three age groups, the grand average ERPs to the target words are characterised by an auditory P1-N1-P2 complex that is followed by a broad negativity (N400). The latter ERPs were elicited during the categorical and the associative priming experiment by both related and unrelated target words, as depicted in Appendices 3 and 4. For the unrelated conditions, the negative deflections seem to be larger (more negative) in comparison to the related conditions, which is indicative of an N400 effect. The shape and timing of the waveforms look similar to those elicited during comparable auditory priming experiments in young and in elderly individuals (Hagoort et al., 1996; Holcomb & Neville, 1990; Räling et al., 2015; Räling et al., 2016).

3.2.1 The P1-N1-P2 complex

Table 6 provides an overview of the statistical results, whereas the normative amplitude and latency data for the sensory components during the categorical and associative priming experiments are provided in Appendix 5 and 7 respectively.

For both priming tasks, the mean amplitudes of the P1 component did not significantly differ between the related and the unrelated condition, and the size of the responses was approximately equal at frontal and at central electrode sites. Interestingly, increasing age affected the size of the P1 amplitudes as revealed by the main effects of age group (categorical priming (CP): $F(2, 104)=3.59$, $p<0.05$; associative priming (AP): $F(2, 104)=9.30$, $p<0.001$). Post hoc comparisons revealed that the elderly showed significantly larger amplitudes than the young during categorical priming (mean difference 0.6 µV, 95% CI [0.02 – 1.1], $p<0.05$), whereas both the middle-aged (mean difference 0.7 µV, 95% CI [0.1 – 1.3], $p<0.05$) and the elderly (mean difference 1.1 µV, 95% CI [0.4 – 1.7], $p<0.001$) showed larger amplitudes than the young during associative priming. Finally, the P1 amplitudes did not significantly differ between men and women, independent of the age group under investigation.

Similar to findings on the P1, the mean amplitudes of the N1 component did not significantly differ between the experimental conditions. The N1 responses were maximal at central electrode sites (main effects of AP-distribution, CP: $F(1,104)=83.45$, $p<0.001$; AP: $F(1, 104)=64.55$, $p<0.001$) and, for associative priming, this was the most clear in the related condition (condition by AP-distribution interaction, $F(1, 104) = 6.19$, $p<0.05$). There were no significant differences between age groups and between genders during both tasks. Conversely, higher onset latencies were found with increasing age as reflected by the corresponding main effects (CP: $F(2, 104)=8.37$, $p<0.001$; AP: $F(2, 104)=16.36$, $p<0.001$). In more detail, post hoc comparisons revealed that a significant onset delay, relative to the young group, occurred from elderly age onwards during categorical priming (mean difference: 9 ms, 95% CI [4 - 15], $p<0.001$), and from middle-age onwards during associative priming (mean difference middle-age – young: 6 ms, 95% CI [0.3 – 11], $p<0.05$; mean difference elderly – young: 14 ms, 95% CI [8 - 20], $p<0.001$). No significant gender-related differences were detected regarding these onset latencies.

Finally, larger mean amplitudes of the P2 component were found in the unrelated than in the related condition during the associative priming task (main effect of condition: $F(1, 104)=6.00$, $p<0.05$). During both priming tasks, the significant main effects of AP-distribution (CP: $F(1, 104)=62.58$, $p<0.001$; AP: $F(1, 104)=42.74$, $p<0.001$) reflected a frontal maximum, that was present in male and female subjects from all age groups. The P2 amplitudes were not significantly different between age groups, but they were larger in women than in men. This difference between genders was observed in all age groups, but was significant only in the elderly individuals (gender by age group interactions, CP: $F(2, 104)=4.16$, $p<0.05$; AP: $F(2, 104)=3.75$, $p<0.05$). Concerning the P2 latencies, the onset did not differ between the experimental conditions during categorical priming, but was earlier for the unrelated than for the related condition during associative priming (main effect of condition: $F(1, 104)=6.21$, $p<0.05$). Main effects of age group were revealed (CP: $F(2, 104)=17.55$, $p<0.001$, AP: $F(2, 104)=18.30$, $p<0.001$) and applied to male participants only for categorical priming (age group by gender interaction: $F(2, 104)=7.12$, $p<0.01$) and to both men and women for associative priming. For the categorical priming task, a significant onset delay relative to the young (male) subjects was present from middle-age onwards ($p<0.05$), whereas for associative priming such a delay was present in both genders from elderly age onwards ($p<0.05$). Moreover, for both tasks, women showed earlier onsets than men (main effects of gender, CP: $F(1, 104)=15.48$, $p<0.001$; AP: $F(1, 104)=10.83$, $p<0.01$), reaching statistical significance in the elderly individuals (age group by gender interactions, CP: $F(2, 104)=7.12$, $p<0.01$, AP: $F(2, 104)=3.20$, $p<0.05$) (Figure 2A and 2B).

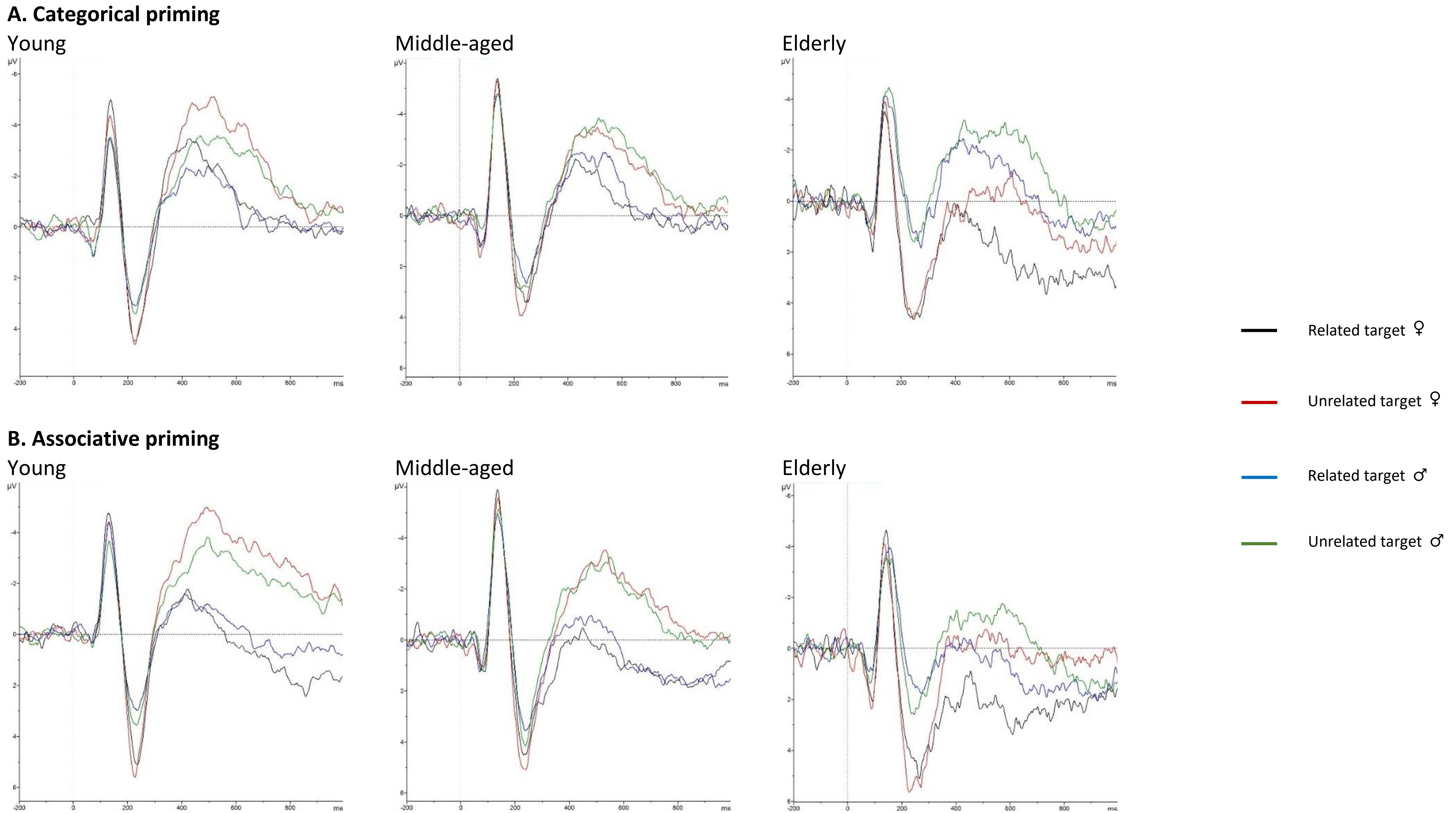


Figure 2: Grand average ERPs of the young (n=40), middle-aged (n=40) and elderly individuals (n=30) elicited during the **A)** categorical priming and **B)** associative priming task at electrode position Cz. In the three age groups, the sensory P1, N1 and P2 components and the semantic N400 component are elicited by related and unrelated target words. In elderly women, the amplitudes of the P2 are significantly larger than in men, for both experimental tasks (µV = microvolt; ms = milliseconds).

Table 6: Repeated measures of **A)** the amplitudes of the P1, N1 and P2 and **B)** the onset latencies of the N1 and P2, elicited during the categorical and associative priming experiment.

ERP	Factor	df	Categorical priming		Associative priming	
			F-values	p-values	F-values	p-values
A. Amplitude (µV)						
P1	Age group (Age)	2, 104	3.59	*	9.30	***
	Gender (Gen)	1, 104	0.02	ns	2.18	ns
	Age x Gen	2, 104	1.99	ns	0.97	ns
	Condition (Con)	1, 104	0.19	ns	0.12	ns
	Con x Age	2, 104	0.67	ns	0.48	ns
	Con x Gen	1, 104	0.94	ns	0.05	ns
	Con x Age x Gen	2, 104	1.97	ns	0.02	ns
	AP distribution (AP dis)	1, 104	3.66	ns	1.27	ns
	AP dis x Age	2, 104	2.40	ns	0.87	ns
	AP dis x Gen	1, 104	0.54	ns	0.16	ns
	AP dis x Age x Gen	2, 104	3.56	*	0.19	ns
	Con x AP dis	1, 104	0.60	ns	3.15	ns
	Con x AP dis x Age	2, 104	0.83	ns	0.56	ns
	Con x AP dis x Gen	1, 104	0.71	ns	0.88	ns
	Con x AP dis x Age x Gen	2, 104	0.41	ns	0.20	ns
N1	Age group (Age)	2, 104	1.80	ns	2.18	ns
	Gender (Gen)	1, 104	0.00	ns	0.04	ns
	Age x Gen	2, 104	1.52	ns	0.48	ns
	Condition (Con)	1, 104	0.03	ns	2.58	ns
	Con x Age	2, 104	0.92	ns	1.06	ns
	Con x Gen	1, 104	0.54	ns	0.72	ns
	Con x Age x Gen	2, 104	0.45	ns	0.23	ns
	AP distribution (AP dis)	1, 104	83.45	***	64.55	***
	AP dis x Age	2, 104	2.01	ns	1.09	ns
	AP dis x Gen	1, 104	1.92	ns	1.24	ns
	AP dis x Age x Gen	2, 104	0.60	ns	0.20	ns
	Con x AP dis	1, 104	0.03	ns	6.19	*
	Con x AP dis x Age	2, 104	0.22	ns	0.95	ns
	Con x AP dis x Gen	1, 104	0.28	ns	0.50	ns
	Con x AP dis x Age x Gen	2, 104	0.04	ns	0.48	ns
P2	Age group (Age)	2, 104	0.28	ns	0.55	ns
	Gender (Gen)	1, 104	14.22	***	15.41	***
	Age x Gen	2, 104	4.16	*	3.75	*
	Condition (Con)	1, 104	0.18	ns	6.00	*
	Con x Age	2, 104	0.44	ns	0.65	ns
	Con x Gen	1, 104	1.12	ns	0.30	ns
	Con x Age x Gen	2, 104	0.04	ns	1.10	ns
	AP distribution (AP dis)	1, 104	62.58	***	42.74	***
	AP dis x Age	2, 104	1.91	ns	0.31	ns
	AP dis x Gen	1, 104	0.01	ns	0.54	ns
	AP dis x Age x Gen	2, 104	2.17	ns	2.08	ns
	Con x AP dis	1, 104	2.76	ns	3.63	ns
	Con x AP dis x Age	2, 104	0.66	ns	0.78	ns
	Con x AP dis x Gen	1, 104	0.11	ns	0.86	ns
	Con x AP dis x Age x Gen	2, 104	0.15	ns	1.13	ns
B. Latency (ms)						
N1	Age group (Age)	2, 104	8.37	***	16.36	***
	Gender (Gen)	1, 104	1.44	ns	0.50	ns
	Age x Gen	2, 104	1.24	ns	0.55	ns
	Condition (Con)	1, 104	0.35	ns	0.68	ns
	Con x Age	2, 104	0.06	ns	2.34	ns
	Con x Gen	1, 104	2.02	ns	0.13	ns
	Con x Age x Gen	2, 104	1.83	ns	0.51	ns
P2	Age group (Age)	2, 104	17.55	***	18.30	***
	Gender (Gen)	1, 104	15.48	***	10.83	**
	Age x Gen	2, 104	7.12	**	3.20	*
	Condition (Con)	1, 104	1.69	ns	6.21	*
	Con x Age	2, 104	0.47	ns	0.06	ns
	Con x Gen	1, 104	0.51	ns	0.12	ns
	Con x Age x Gen	2, 104	0.21	ns	0.95	ns

Note: µV = microvolt; ms = milliseconds; ERP: event-related potential; df: degrees of freedom; * p < 0.05; ** p < 0.01; *** p < 0.001; ns: non-significant

3.2.2 The N400(-effect)

A summary of the statistical results can be found in Table 7. In general (i.e. across conditions and across the nine electrode positions of interest), a comparison of the N400 amplitudes in a broad time window (300-800 ms) revealed more positive (less negative) activity with increasing age (main effects of age group, CP: $F(2, 104)=10.27$, $p<0.001$; AP: $F(2, 104)=13.53$, $p<0.001$). Post hoc comparisons showed, in comparison to the young, significant less negative activity in the elderly for categorical priming (mean difference: 1.9 µV, 95% CI [0.9 – 2.9], $p<0.001$) and in both the middle-aged (mean difference: 1.1 µV, 95% CI [0.2 – 1.9], $p<0.05$) and the elderly (mean difference: 2.0 µV, 95% CI [1.1 – 3.0], $p<0.001$) for associative priming. However, for categorical relationships, this only applied to elderly women as they had significantly more positive activity in comparison to elderly men (age group by gender interaction: $F(2, 104)=5.29$, $p<0.01$). Importantly, men and women of the three age groups showed significant N400 priming effects, characterised by more negative (or less positive) amplitudes for the unrelated than for the related targets (main effects of condition, CP: $F(1, 104)=109.36$, $p<0.001$, AP: $F(1, 104)=209.89$, $p<0.001$). No condition by age group interactions could be detected. For associative relationships, women showed more facilitation (less negative amplitudes) for related targets in comparison to men, whereas the responses elicited by unrelated targets were of similar size in both genders (condition by gender interaction: $F(1, 104) = 6.05$, $p<0.05$). Accordingly, a univariate ANOVA revealed that the size of the main N400 effects (300-800 ms), as measured in the difference waves (unrelated minus related responses), was not significantly affected by ageing for both types of relationships (Figure 3A and 3B). Though, larger associative priming effects were elicited in women than in men as observed across all age groups (main effect of gender: $F(1, 104) = 6.05$, $p<0.05$) (Figure 2B and 4B).

Moreover, the associative N400 effect was significantly larger in comparison to the categorical N400 effect (-1.9 µV versus -1.1 µV, main effect of target type: $F(1, 104) = 34.40$, $p<0.001$).

The latter difference was independent of gender and age group. Appendices 3 and 4 represent the grand average ERPs elicited by the related and unrelated targets at frontal, central and parietal electrode sites for the categorical and associative priming task respectively.

In order to investigate possible timing-related differences in the N400 priming effect between the three age groups and between genders, temporally more refined comparisons were performed. More precisely, the amplitudes of the difference waves were measured in five time-windows of 100 ms each, namely 300-400 ms, 400-500 ms, 500-600 ms, 600-700 ms and 700-800 ms (Räling et al., 2016), and time-window was used as a within-subject variable in the repeated-measures ANOVA (Iragui et al., 1996). For the categorical priming task, no significant interaction between time window and age group was detected (Figure 3A). In the three age groups, the size of the N400 effect increased until 700 ms and decreased thereafter (main effect of time window, $F(2.6, 269.0) = 57.20$, $p<0.001$). Although women tended to show larger N400 effects than men from 400 ms on, the main effect of gender or the time-window by gender interaction was not significant (Figure 4A). Regarding associative priming, the size of the N400 effect increased until 600 ms, remained stable between 600-700 ms and was followed by a decrease thereafter (main effect of time-window: $F(2.9, 304.6)=51.02$, $p<0.001$). However, the latter only holds true for the elderly individuals since the young and the middle-aged subjects showed similar amplitudes between 600-700 ms and 700-800 ms. Accordingly, the time window by age group interaction ($F(5.9, 304.6) = 3.51$, $p<0.01$) reflected a significantly smaller N400 effect between 700-800 ms in the elderly in comparison to the young participants (Figure 3B). Interestingly, a larger associative priming effect in women than in men was present across all time-windows as shown by the significant main effect of gender ($F(1, 104) = 6.03$, $p<0.05$) and a lacking time window by gender interaction (Figure 4B). Appendix 6 provides an overview of the normative data for the amplitudes of the N400 priming effect (collapsed across frontal, central and parietal electrode sites) for the categorical (part A) and the associative experiment (part B) in each time window, for both men and women from the three age groups.

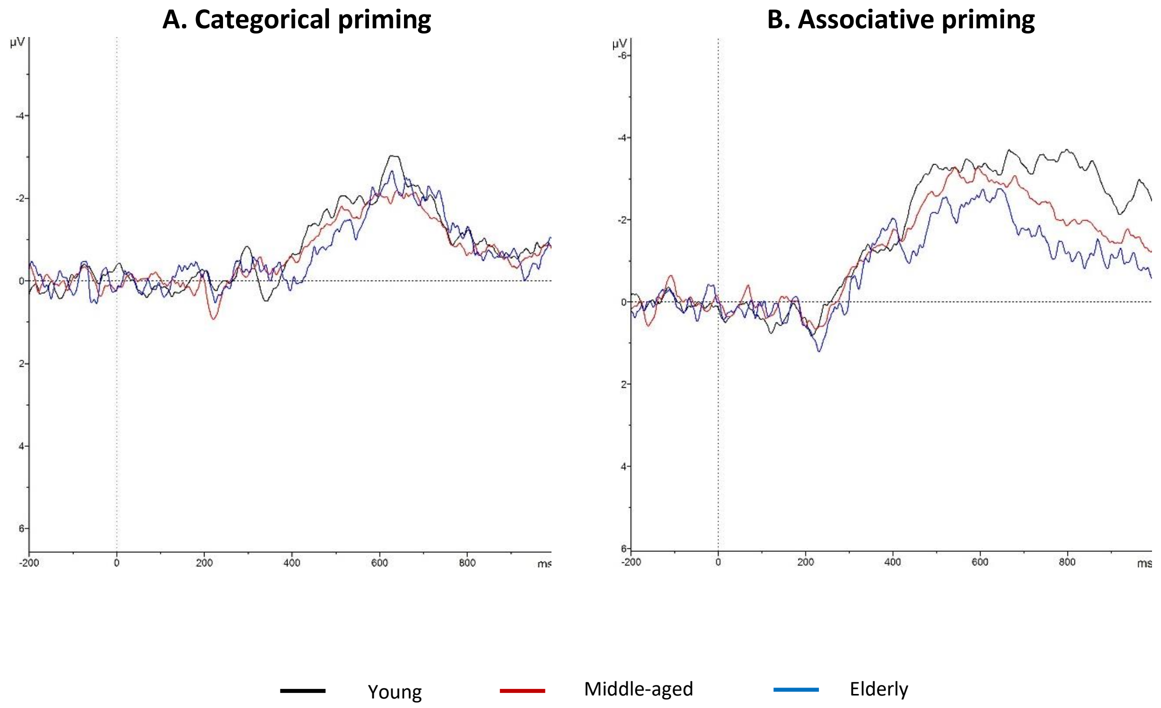
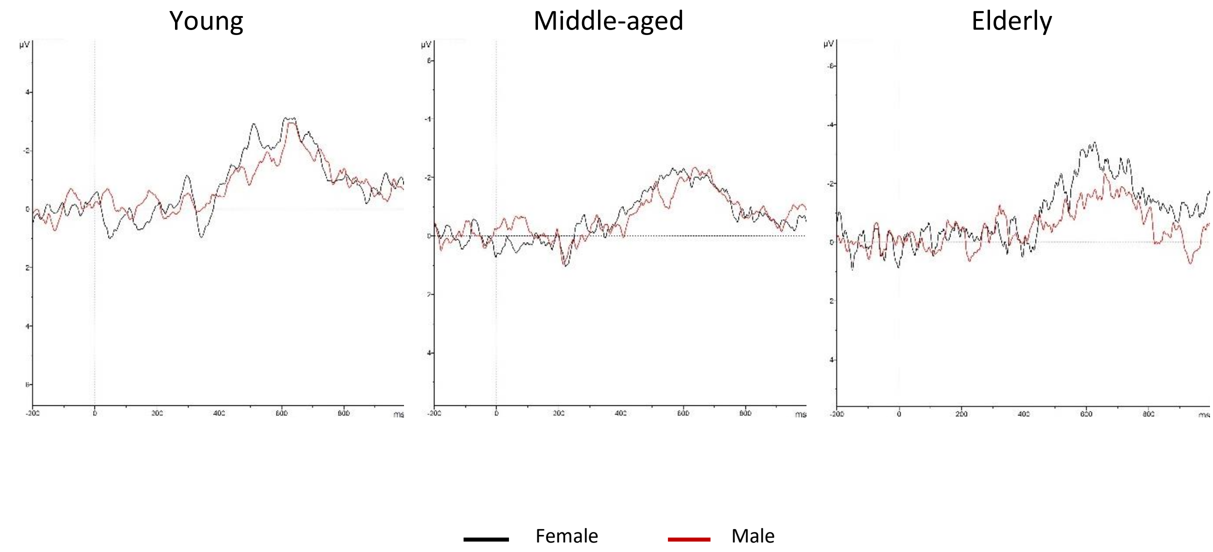


Figure 3: Grand average difference waveforms of the young (n=40), middle-aged (n=40) and elderly individuals (n=30) elicited during the **A)** categorical priming and **B)** associative priming task at electrode position Cz. For both tasks, the mean amplitudes in the time-window 300-800 ms were not significantly different between age-groups. For associative priming, elderly participants did show significant smaller mean amplitudes in the time-window 700-800 ms in comparison to the young individuals (µV = microvolt; ms = milliseconds).

A. Categorical priming



B. Associative priming

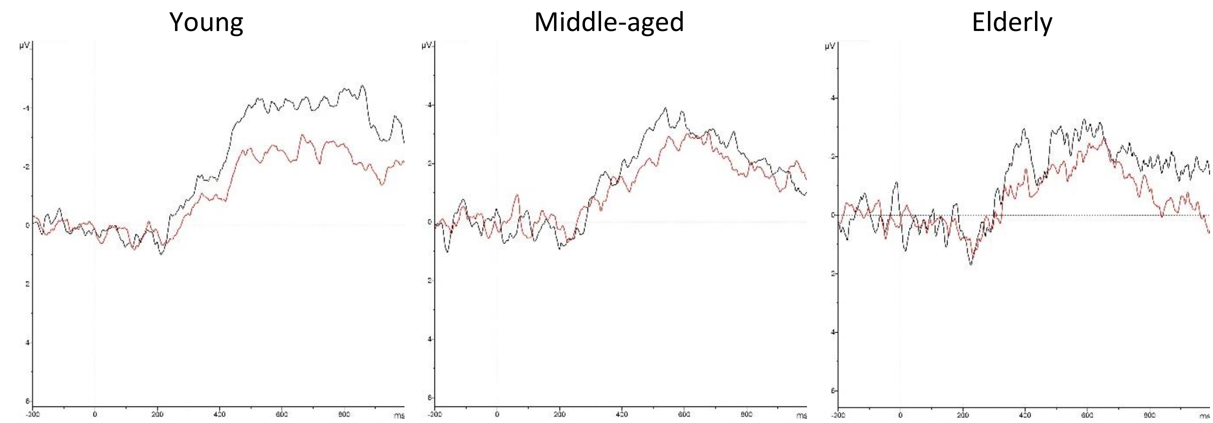


Figure 4: Grand average difference waveforms of female and male subjects of the young (20 ♀ and 20 ♂), middle-aged (20 ♀ and 20 ♂) and elderly age group (15 ♀ and 15 ♂) elicited during the **A)** categorical priming and **B)** associative priming task at electrode position Cz. For associative priming, women elicited significantly larger N400 effects in comparison to men (µV = microvolt; ms = milliseconds).

Focusing on the N400 latencies (Appendix 7), the young group showed a more rapid onset for categorically related than for unrelated items (condition by age group interaction: $F(2, 104)=4.62$, $p<0.05$). A similar phenomenon seemed to be present during the associative priming task in young women, but this did not reach statistical significance. For associative priming, a main effect of age group was detected ($F(2, 104) = 4.19$, $p<0.05$). Post hoc comparisons revealed significantly earlier onsets for the elderly in comparison to the young (mean difference: 22 ms, 95% CI [3 - 42], $p<0.05$). This result seemed to be driven by the unrelated condition during which multiple young (but less older) individuals showed large amplitudes in the later time-windows. As fractional (20%) area latencies were used to determine the onset of the N400, this might provide an explanation for this rather unexpected finding. Lastly, no significant gender-related effects were found for either task. Regarding the N400 effects, the associative N400 effect seemed to have an earlier onset than the categorical priming effect, but this observation missed statistical significance. Considering task-specific ageing and gender effects, the categorical N400 effect was characterised by higher onset latencies with increasing age. However, the mean latency differences between age groups were not significant. In addition, no significant onset latency differences between male and female individuals were detected, for neither age group. For associative priming, the onset latencies showed a small decrease in the elderly compared to the young and middle-aged subjects (similar to findings on the N400 latency). This result seems to be driven especially by the women. Nevertheless, these findings were not borne out by significant main effects nor by significant interactions.

Finally, the topographical distributions of the categorical and of the associative N400 effects were mainly similar (Appendix 8). Across all age groups and both genders, the categorical and associative N400 priming effects between 300-800 ms were largest over centro-parietal areas, and smallest in amplitude over frontal areas (main effects of AP-distribution, CP: $F(1.3, 139.6) = 40.84$, $p<0.001$; AP: $F(1.3, 132.9) = 46.11$, $p<0.001$). For associative priming, the difference between central and frontal activity was larger in female than in male participants (AP-distribution by gender interaction, $F(1.3, 132.9) = 3.68$, $p<0.05$). Regarding the lateralisation pattern of categorical priming, both young, middle-aged and elderly showed larger amplitudes at the midline than at left and right hemispheric sites, which were characterised by similar amplitudes (main effect of lateralisation: $F(1.7, 172.8) = 11.69$, $p<0.001$). Interestingly, the aforementioned lateralisation pattern was present at anterior and central regions but changed towards the posterior electrodes. More precisely, for posterior regions only, the size of the N400 effect was similar at left-sided and at midline regions and, hence, significantly larger at the left compared to the right hemisphere (AP-distribution by lateralisation interaction: $F(3.1, 326.0) = 6.02$, $p<0.001$). Importantly, for categorical priming, no significant interactions were found between AP-distribution or lateralisation and age group or gender, suggesting a similar topographical distribution across age groups and genders. In comparison to the aforementioned results, the lateralisation characteristics for associative priming were slightly different. The main effect of lateralisation ($F(1.7, 178.2) = 33.94$, $p<0.001$), reflected the largest amplitudes at the midline, but intermediate at the right and lowest at the left side. The latter held true for the anterior and central regions, whereas posterior effects showed a more symmetrical distribution among the left and right hemisphere (AP-distribution by lateralisation interaction: $F(2.5, 259.8) = 7.74$, $p<0.001$). Moreover, the main lateralisation effect only applied to the middle-aged individuals. Young individuals showed equivalent left and right hemispheric effects, whereas elderly showed significantly larger right than left effects ($p<0.001$). Hence, for associative priming, the N400 effect tended to become more pronounced at right than at left hemispheric regions with increasing age (lateralisation by age group interaction: $F(3.4, 178.2) = 3.77$, $p<0.01$). The latter findings applied to both men and women.

Table 7: Overview of the statistical results on the amplitudes and onset latencies of the N400 and on the amplitudes, onset latencies and topography of the N400 effect, elicited during the categorical and associative priming experiment.

A. Amplitude (μV)

ERP	Factor	df	Categorical priming (CP) F-values	Categorical priming (CP) p-values	Associative priming (AP) F-values	Associative priming (AP) p-values
N400 (300-800 ms)	Age group (Age)	2, 104	10.27	***	13.53	***
	Gender (Gen)	1, 104	3.60	ns	1.94	ns
	Age x Gen	2, 104	5.29	**	2.07	ns
	Condition (Con)	1, 104	109.36	***	209.89	***
	Con x Age	2, 104	0.05	ns	2.28	ns
	Con x Gen	1, 104	1.41	ns	6.05	*
	Con x Age x Gen	2, 104	0.28	ns	0.64	ns
N400 effect (300-800 ms)	Age group (Age)	2, 104	0.05	ns	2.28	ns
	Gender (Gen)	1, 104	1.41	ns	6.05	*
	Age x Gen	2, 104	0.28	ns	0.64	ns

ERP	Factor	df CP	df AP	CP F-values	CP p-values	AP F-values	AP p-values
N400 effect (5 time-windows)	Age Group (Age)	2, 104	2, 104	0.05	ns	2.24	ns
	Gender (Gen)	1, 104	1, 104	1.45	ns	6.03	*
	Age x Gen	2, 104	2, 104	0.28	ns	0.63	ns
	Time-window (Time)[a]	2.6, 269.0	2.9, 304.6	57.20	***	51.02	***
	Time x Age[a]	5.2, 269.0	5.9, 304.6	1.95	ns	3.51	**
	Time x Gen[a]	2.6, 269.0	2.9, 304.6	2.02	ns	0.99	ns
	Time x Age x Gen[a]	5.2, 269.0	5.9, 304.6	0.50	ns	0.99	ns

B. Latency (ms)

ERP	Factor	df	CP F-values	CP p-values	AP F-values	AP p-values
N400 (300-800 ms)	Age group (Age)	2, 104	1.05	ns	4.19	*
	Gender (Gen)	1, 104	1.32	ns	3.80	ns
	Age x Gen	2, 104	0.18	ns	0.39	ns
	Condition (Con)	1, 104	0.34	ns	1.23	ns
	Con x Age	2, 104	4.62	*	2.29	ns
	Con x Gen	1, 104	0.60	ns	1.39	ns
	Con x Age x Gen	2, 104	0.32	ns	1.29	ns
N400 effect (300-800 ms)	Age group (Age)	2, 104	0.15	ns	2.34	ns
	Gender (Gen)	1, 104	0.02	ns	0.47	ns
	Age x Gen	2, 104	1.53	ns	0.16	ns

C. Topography

ERP	Factor	df CP	df AP	CP F-values	CP p-values	AP F-values	AP p-values
N400 effect (300-800 ms)	Age group (Age)	2, 104	2, 104	0.05	ns	2.28	ns
	Gender (Gen)	1, 104	1, 104	1.41	ns	6.05	*
	Age x Gen	2, 104	2, 104	0.28	ns	0.64	ns
	AP-distribution (AP dis)[a]	1.3, 139.6	1.3, 132.9	40.84	***	46.11	***
	AP dis x Age[a]	2.7, 139.6	2.6, 132.9	0.34	ns	0.63	ns
	AP dis x Gen[a]	1.3, 139.6	1.3, 132.9	0.79	ns	3.68	*
	AP dis x Age x Gen[a]	2.7, 139.6	2.6, 132.9	0.67	ns	0.91	ns
	Lateralisation (Lat)[a]	1.7, 172.8	1.7, 178.2	11.69	***	33.94	***
	Lat x Age[a]	3.3, 172.8	3.4, 178.2	1.10	ns	3.77	**
	Lat x Gen[a]	1.7, 172.8	1.7, 178.2	0.01	ns	0.16	ns
	Lat x Age x Gen[a]	3.3, 172.8	3.4, 178.2	0.30	ns	0.16	ns
	AP dis x Lat[a]	3.1, 326.0	2.5, 259.8	6.02	***	7.74	***
	AP dis x Lat x Age[a]	6.3, 326.0	5.0, 259.8	1.20	ns	1.23	ns
	AP dis x Lat x Gen[a]	3.1, 326.0	2.5, 259.8	2.75	ns	2.42	ns
	AP dis x Lat x Age x Gen[a]	6.3, 326.0	5.0, 259.8	1.24	ns	1.03	ns

Note: μV = microvolt; ms = milliseconds; ERP: event-related potential; df: degrees of freedom; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; ns: non-significant; [a] : Greenhouse-Geisser corrected degrees of freedom, F-values and p-values.

3.3 Correlations between electrophysiological and behavioural measures

A significant negative correlation was found between the size of the associative N400 effect and the corresponding behavioural accuracy (Spearman's rho= -0.2 , $p<0.05$), showing that larger N400 effects (more negative) accompanied higher accuracy levels. For the categorical priming measures, the correlations did not reach statistical significance.

4. Discussion

In the current study, we aimed to investigate the effects of healthy ageing and gender on the processing of categorical and associative relationships between auditorily presented words. One hundred and ten individuals (55 men and 55 women), divided among three age groups (young, middle-aged and elderly), were subjected to two semantic priming paradigms during an EEG registration. The observed ageing and gender effects on the elicited ERPs are discussed in the first and second section of the discussion respectively. Moreover, we had the opportunity to develop normative electrophysiological data. The purpose of the latter data will be discussed in the final section.

4.1 Effects of healthy ageing on the processing of semantic relationships

In general, previous research towards healthy ageing effects on cognitive skills, including semantic processing, is dominated by cross-sectional comparisons of adults in their 20's and adults above 60 years. Relatively little information is available about the age-related changes that occur in middle-aged subjects (Finch, 1991; Hedden & Gabrieli, 2004; Raz, 2009). In the current study, we addressed this shortcoming by expanding the sampled age range under investigation. In both the young (20-39 years), the middle-aged (40-59 years) and the elderly individuals (>60 years), an auditory P1-N1-P2-complex, and a broad negativity, the N400, was elicited by categorically and associatively related and unrelated target words.

P1-N1-P2 complex – Independent of gender, early cortical processing of the auditory verbal stimuli was modulated by healthy ageing as reflected by the significantly enhanced P1 amplitudes in elderly subjects (categorical priming), or in both middle-aged and elderly individuals (associative priming), in comparison to the youngest group. These fronto-central amplitude increments with increasing age could be related to the general theory of age-related changes (reductions) in neural inhibition (Caspary, 2008; Willott, 1996). Another possibility, however, could be that increasing age was associated with some form of high-frequency hearing loss (i.e. presbyacusis). Even though all participants indicated that they understood the presented words well, (mild) hearing loss might have occurred as an audiometric evaluation was not part of our experimental protocol. (Slight) changes in high frequency hearing ability might induce neural reorganization of the auditory cortex with a larger representation of low and mid-range frequencies that are of utter importance for speech. As such, listening to words might have addressed a larger amount of synchronously firing neurons in (middle-aged and) older participants, leading to the enhanced amplitudes in comparison to the young (Sörös et al., 2009; Tremblay et al., 2003). On the contrary, we did not observe significant amplitude changes for the N1 and P2 components (for men nor for women), corresponding to findings of previous studies using verbal stimuli during attentive listening conditions (Federmeier et al., 2003; Giaquinto et al., 2007; Woodward et al., 1993). A second manifestation of increasing age was a significant delay in the onset latencies of the N1 and P2, as observed during both priming tasks. Depending on the experimental ERP-task, these delays were present from middle-age (N1: associative priming, P2: categorical priming) or elderly age (N1: categorical priming, P2: associative priming) onwards or could be detected in male participants only (P2: categorical priming). Prolonged peak latencies of the P2, elicited by auditorily presented words, are regularly described, but results for the N1 are less clear (Federmeier et al., 2003; Giaquinto et al., 2007; Woodward et al., 1993). Nonetheless, our current findings support the series of observations by Tremblay and colleagues regarding the auditory processing of speech stimuli. These authors compared the effects of stimulus complexity (pure tones versus speech syllables) on the peak latency of the P1, N1 and P2 in healthy young (n=10) and older participants (n=10). With a similar inter-stimulus interval (910 ms) as in our ERP-tasks (800 ms), elderly subjects showed delayed N1 and P2 *peak* latencies for the speech syllables (see also Tremblay et al., 2002), but not for the pure tones (Tremblay et al., 2004). In our study, similar results were found for the *onset* latencies of these components. Altogether, evidence is accumulating that increasing age results in prolonged (peak and onset) latencies of the N1-P2 complex during speech processing and that such delays might be present from middle-age onwards. The latter findings have been associated with age-related differences in the refractory period of auditory evoked potentials, namely a faster neural recovery cycle in young individuals (Papanicolaou et al., 1984; Tremblay & Ross, 2007; Tremblay et al., 2004; Tremblay et al., 2002). In the context of speech processing, auditorily presented words consist of rapidly occurring acoustic changes, each of them eliciting P1-N1-P2 responses. If the auditory system of older subjects needs more time to recover from the initial excitations before neuronal firing can occur again, this might contribute to delays along the cortical auditory processing stream of speech stimuli (Rufener et al., 2014; Tremblay & Ross, 2007).

The N400 effect - For both types of semantic relationships, a significant N400 priming effect (N400 amplitudes unrelated condition > N400 amplitudes related condition) was present in the three age groups. This persistence of a processing benefit for semantically related words corresponds to the general view that semantic memory remains relatively intact with increasing age (Park et al., 2002; Federmeier et al., 2002). In accordance with preceding findings in the literature (Hutchison et al., 2008; Sachs et al., 2008b), priming effects were larger for associative than for categorical relationships. Moreover, the former relationships were characterised by an earlier onset of the N400 priming effect, although missing statistical significance. These results suggest that associative relationships are activated more efficiently than categorical ones (see also Kutas and Iragui, 1998), possibly due to their lower cognitive demands (Belacchi & Artuso, 2018; Sachs et al., 2008a).

Based upon previous research towards ageing effects on the N400 effect elicited by word pairs in the auditory modality (Federmeier et al., 2003; Räling et al., 2016), one could carefully suggest that the categorical N400 effect is more prone to increasing age than the associative N400 effect. In the current study, the latter hypothesis was not confirmed, as we did not observe significant amplitude differences between the three age groups during the categorical priming task. The mean amplitudes in the broad time-window of 300-800 ms, and within the smaller time-windows of 100 ms (300-400 ms, 400-500 ms, 500-600 ms, 600-700 ms, 700-800 ms) remained stable in the young, middle-aged and elderly subjects under evaluation. During the associative priming task, the N400 effect tended to decrease for the elderly between 300-800 ms, but differences were only significant in the time-window of 700-800 ms. The finding of absent ageing effects for categorical priming seems to be rather unexpected considering the obtained behavioural results. More precisely, elderly subjects had lower accuracies for the explicit categorical relationship judgements (button press responses), in comparison to the young and the middle-aged participants. There was, however, no significant correlation between the size of the N400 categorical priming effect and the corresponding behavioural accuracy, in contrast to findings for the associative priming experiment.

For associative priming, our findings mainly agree with those of Federmeier et al. (2003) who found no age-related differences in the amplitude of the corresponding N400 effect (time-windows 200-400 ms, 400-600 ms and 600-800 ms). Our deviating observation of significantly reduced amplitudes between 700-800 ms for elderly participants in comparison to the young might be due to the analysis of a different amplitude parameter (mean amplitude) and/or different time-windows (100 ms sub-windows) than Federmeier and colleagues (peak amplitude and 200 ms sub-windows).

Regarding categorical priming, ageing-resistant N400 effects seem to contradict the findings of Räling et al. (2016), who reported on absent N400 effects at centro-parietal electrode sites in elderly individuals. As such, our findings do not support the IDH (Hasher & Zacks, 1988) on the semantic domain. This discrepancy could have been caused by methodological differences regarding the linguistic ERP-paradigm. In Räling et al. (2016), an auditory category-member verification task was used to investigate the influence of age of acquisition (AoA) and typicality (TYP) on semantic processing in the ageing brain (and in patients with aphasia). Hence, the task consisted of a smaller amount of unrelated (n=80) than related trials (n=160) with the target words significantly differing regarding their AoA and TYP. The semantic priming (N400) effect was mainly used as a control condition. Conversely, the influence of ageing (and gender) on the latter effect was the main focus in the current study. Our target words from the related (n=60) and unrelated condition (n=60) were matched on psycholinguistic variables (e.g. word frequency, phonological length, concreteness, age of acquisition, valence, arousal, dominance etc.) that could affect the amplitudes of the N400 and of components in earlier time-windows (Adorni et al., 2013; Assadollahi & Pulvermüller, 2003; Hauk & Pulvermüller, 2004; Pulvermüller et al., 2009). In the context of healthy ageing research, this accurate matching procedure is necessary as there is increasing evidence that certain features are processed differently in older-aged persons (De Deyne & Storms, 2007; Molnár et al., 2013; Räling et al., 2016). For example, a significant N400 effect for negative, but not for positive words has been observed in elderly subjects (Molnár et al., 2013). Likewise, Räling et al (2016) themselves found inversed AoA-effects (i.e. more negative amplitudes for early than for late acquired words) within the N400 latency range in the older adults under investigation. Probably, this may have influenced the size of their N400 effect. Although more research is required on this domain, variables that are not the main focus of an experiment should definitely be controlled for when investigating the influence of ageing on the N400 effect. In previous studies (including those targeting semantic priming in the visual modality), some of the aforementioned features have been controlled for, but other characteristics (e.g. age of acquisition, valence, arousal, dominance) have not been considered. In such cases, it might be possible that reductions of the N400 effect in elderly are due to age-related processing differences regarding certain characteristics of the stimulus items, instead of them being (completely) related to semantic priming. To the best of our knowledge, our study is the first in which (almost) all of the (currently) known variables were considered. Thus, a (dis)confirmation of our findings by future studies requires an extensive monitoring of psycholinguistic variables among the experimental conditions.

In contrast to the significant onset delays of the auditory N1 and P2 components, no significant onset difference between age groups was found for both N400 priming effects. These findings do not correspond to the general slowing hypothesis (Salthouse, 1996) or to the prediction that older adults need more to time to search within larger semantic networks (Cohen, 1990; Kutas & Iragui, 1998). In previous research, the influence of increasing age on the onset time of the N400 effect (elicited by word-pairs) has only been investigated in multimodal priming tasks (i.e. auditorily presented context phrases/primes followed by orthographically presented target words; Iragui et al., 1996; Kutas & Iragui, 1998), revealing a significant delay. Our results show, however, that the onset of the N400 effect is not delayed when no switch between input modalities is required. Moreover, we found that sensory delays (N1 and P2) do not have to result in a delayed onset of cognitive operations (N400 effect), at least for tasks with minimal working memory demands. Similar results have been described at sentence level when participants could benefit from co-articulatory and intonational information during the processing of natural speech (Federmeier et al., 2003).

Finally, the topographical distribution of the categorical and associative N400 effect was characterised by a centro-parietal maximum in the three age groups. Regarding the anterior-to-posterior distribution, we did not find any support for an age-related increase of anterior (frontal) activity and reduction of posterior activity (PASA model, Davis et al., 2008), this in contrast to previous results on categorical priming (Räling et al., 2016). Our findings correspond well to the results of a recent meta-analysis on age-related functional changes in semantic neural networks (Hoffman & Morcom, 2018). The latter study, however, included tasks with a wide variety of experimental stimuli (e.g. written and spoken words, pictures and odours). Hence, for auditory semantic priming, more research is needed to clarify the application of the PASA model. Second, the categorical N400 effect was characterised by a left-hemispheric lateralisation pattern for the posterior areas, but no left or right predominance for the anterior and central areas. No lateralisation differences between the three age groups were observed for this task. Remarkably, the absence of significant age-related topography changes for categorical priming was accompanied by significantly lower behavioural accuracy scores. Conversely, Räling et al. (2016) observed a shift from a bilateral (centro-parietal) N400 effect in the young towards a right (frontal) effect in the elderly, along with similar accuracy scores in both age groups. The combination of our and Räling's findings raises the question whether a topographical (i.e. lateralisation or anterior-to-posterior distribution) shift during categorical priming is required to maintain the young-like behavioural outcome. The results from the associative priming task seem to support this hypothesis. In more detail, the associative N400 effect tended to become more pronounced at right than at left hemispheric regions from middle-age onwards. These findings support the theory of a hemispheric asymmetry reduction in older adults (HAROLD; Cabeza, 2002; Hoffman & Morcom, 2018; Räling et al., 2016) and could be compensatory in nature since no significant ageing differences were observed among the corresponding behavioural accuracy scores. In previous research, Federmeier and colleagues did not observe age-related topography changes for the auditory associative N400 effect (Federmeier et al., 2003), but information on the behavioural accuracy scores is, however, not available as participants were not required to explicitly judge the associative relationships. Altogether, whether or not a topographical shift supports intact categorical and associative priming in older individuals should be confirmed in future research that compares the topography of the (categorical and associative) N400 effect between two groups of older adults with different behavioural performance levels (i.e. similar versus significantly lower accuracy scores than young individuals).

4.2 Effects of gender on the processing of semantic relationships

Differences between men and women in behavioural studies on verbal processing have been frequently reported, with women often being superior on verbal learning and memory tasks (Herlitz & Rehnman, 2008; Kimura, 2002; Maitland et al., 2004; McCarrey et al., 2016; Munro et al., 2012). Through years, structural (Good et al., 2001; Sowell et al., 2007) and functional (Baxter et al., 2003; Kansaku et al., 2000; Konrad et al., 2008; Vikingstad et al., 2000) dissimilarities between the linguistic cortices of men and women have been proposed as explanations for the observed behavioural differences, but conclusive evidence remains lacking (Wallentin, 2009). According to the majority of spatial imaging studies, male and female individuals seem to activate the same core regions of semantic networks without clear lateralisation differences between both genders (Chang et al., 2018; Frost et al., 1999; Nenert et al., 2017; Sommer et al., 2004; Sommer et al., 2008; Xu et al., 2020). In line with the latter, the current ERP-study did not reveal significant topographical differences between men and women, for both the categorical and the associative priming task (see also Wirth et al., 2007).

Interestingly, the hypothesis that men and women use different cognitive strategies to process (verbal) information has gained prominence. In comparison to men, women are suggested to have a lower threshold for the elaborative processing of meaningful (verbal) information. Previous studies found that men are more likely to rely upon a selective subset of salient cues, whereas women engage in a more detailed semantic elaboration of information (Meyers-Levy & Sternthal, 1991). The latter cognitive strategy can lead to higher behavioural scores for verbal tasks in women than in men, but this will largely depend upon the external task demands. For example, women may benefit from a thorough semantic analysis during verbal-episodic memory tasks (e.g. delayed recall and word recognition) due to their increased attention to semantic features and to interrelationships among words (Guillem & Mograss, 2005), resulting in a consistent female advantage on this type of tasks (Herlitz & Rehnman, 2008; Maitland et al., 2004). However, no behavioural differences might be yielded for tests that explicitly target semantic memory, during which a more shallow semantic analysis seems to be sufficient. The latter might provide one explanation for the heterogeneity among behavioural results in the literature, as well as for the current observation of very similar accuracy scores among men and women on the SAT-subtests (verbal association and oral naming) and during the ERP-tasks (explicit button press responses).

The hypothesis of different cognitive strategies in men and in women is supported by our observation of larger N400 effects in females than in males during both ERP-tasks. Although this phenomenon was present in both tasks across age groups, significance was reached solely for the associative priming experiment. Moreover, the onset of processing categorically related targets was earlier in comparison to unrelated targets in both young men and women (see also Wirth et al., 2007), but, during associative priming, such a trend was observed in young females only. Our results are in line with the findings of Daltrozzo et al. (2007), who applied a similar priming task as we did, although no explicit judgement was required regarding the associative relationships in their study. We extended their (marginally significant) results by showing that the amplitude enhancement of the N400 effect in women is not limited to the frontal electrode positions, but is present over centro-parietal sites as well. Larger N400 effects in women, and a faster processing of related targets in young females support the hypothesis that female individuals direct more attention to semantic analysis, as previously reported by Wirth et al. (2007) based upon findings from a visual word priming task. It is well known that the N400 (effect) is modulated by the focus of attention, since the N400 priming responses increase when participants are explicitly instructed to focus on semantic features or relationships (Bentin et al., 1993; Erlbeck et al., 2014). For example, N400 effects can be elicited by processing related and unrelated word pairs during a letter search task, but its size increases when an explicit judgement on their semantic relationship is required (Kutas & Van Petten, 1988). Additional support for this interpretation is provided by the results from an auditory wh-question-answer paradigm, targeting the effects of external cues, namely context/focus (wh-question) and accentuation (answer), on the N400 effect. In male subjects, a significant N400 effect was present only when the context-induced focus in the question and the accentuation in the answer corresponded to each other, whereas female subjects showed similar N400 effects independent of the match between context and accentuation. Hence, the extent of semantic elaboration seemed to be higher in women than in men as the former consistently processed the target words, even if they did not occur in the focus position or were not correctly accentuated (Wang et al., 2011). Altogether, our ERP-results indicate that, even though all the participants were explicitly instructed to focus on the semantic features and relationships, women performed the semantic analysis of (target) words in a more extensive way. For our specific ERP-tasks, however, this cognitive strategy was not beneficial, nor detrimental, as women did not have better or worse button press accuracy scores in comparison to men.

Finally, women also showed larger and earlier P2 responses than men. The latter phenomenon was present in all age groups, but only reached statistical significance in the elderly. The P2 has often been referred to as the "tail end" of the auditory P1-N1-P2 complex, although it should be considered as an independent component, distinct from the N1 (Crowley & Colrain, 2004). It is clear that the P2 is an obligatory response to auditory stimuli (Friedman, 2012), however, its exact functional significance remains rather unclear. Generators in the auditory association cortices have been suggested (Godey et al., 2001), implying that the P2 is related to more complex auditory processing (Stothart & Kazanina, 2016). Moreover, occurring relatively late in the cortical auditory processing stream, the P2 is characterised by a great sensitivity to top-down regulation. Within the context of auditory word processing, multiple studies found phonological, lexical and semantic effects in the latency range of the P2 and even ahead of it (Bentin et al., 1985; Menning et al., 2005; Shtyrov & Pulvermüller, 2007; Stuellein et al., 2016, for a review see Pulvermüller et al., 2009). Such early effects support parallel models of language comprehension that suggest a simultaneous access to phonological, lexical, semantic and syntactic information (Pulvermüller et al., 2009). Hence, higher cognitive processes, such as lexico- semantic access, are suggested to occur within the early latency ranges. This might explain why we observed significantly larger P2 amplitudes for the (associatively) unrelated condition (similar to Holcomb & Neville, 1990 and Woodward et al., 1993).

The enhancement of P2 amplitudes in female subjects might indicate that their deeper level of semantic word processing initiates from early lexico-semantic processing stages on, and is not limited to their more detailed semantic elaboration as revealed in the later time-windows (N400 effect). The exact reason why elderly women in particular showed increases of the P2 in comparison to elderly men remains uncertain, but could be due to "the existence of an ageing-related progressive deficit in the capacity to withdraw attentional resources from stimuli" (García-Larrea et al., 1992). Finally, the onsets of the P2 responses were earlier in the female subjects, reaching significance in the elderly, but this advantage was not carried over to the onsets of the N400 effects, as these were not subjective to significant gender effects. The latter finding seems to contradict Daltrozzo et al. (2007) and Wirth et al., (2007), who reported on significant earlier onsets in women. Unfortunately, the use of peak latencies (Daltrozzo et al., 2007) and topographic analyses (Wirth et al., 2007) to examine the onset of the N400 effect, prevents a valid comparison with fractional area latencies (as used in the current study), and might underlie the contrasting results.

4.3 The clinical value of normative electrophysiological data for auditory semantic priming

The final aim of this study was to provide normative electrophysiological data that are intended to be useful for clinical purposes in Flemish patients with acquired language disorders. The clinical value of ERPs in patients with aphasia primarily depends on 1) their test-retest reliability, 2) their single-subject sensitivity and 3) their sensitivity to sensory and linguistic deficits. Regarding the N400 component, the amplitudes at different evaluation moments are characterised by moderate to high correlations (Kiang et al., 2013; Lew et al., 2007), whereas this adequate reliability over retest intervals remains to be confirmed for the latency measures (Lew et al., 2007). Second, the single-subject sensitivity of the N400 seems to be largely depending on the experimental design as reported by Cruse and colleagues. More specifically, active task demands and word-pair tasks based upon normative associations have been described to increase the likelihood of a significant priming effect in individual participants (Cruse et al., 2014). Thus, our semantic ERP-paradigms meet both conditions well since explicit button press responses were required to judge semantic relationships and Dutch prototypicality and word association norms (de Groot, 1980; de Groot & De Bil, 1987; Lauteslager et al., 1986, Noordman-Vonk, 1977) were used to generate the prime-target pairs. Third, the N400 is highly related to the integrity of semantic knowledge and can differentiate aphasic patients with mild comprehension deficits from patients with moderate to severe deficits. In more detail, the largest N400 amplitude reductions have been observed in patients with moderately to severely affected comprehension skills (Hagoort et al., 1996; Kawohl et al., 2010; Swaab et al., 1997), whereas prolonged N400 latencies can occur independent of the severity of comprehension disorders (Kawohl et al., 2010; Swaab et al., 1997). Altogether, these results provide clear evidence for the clinical value of the N400 component, such that the developed ERP tasks could be useful in longitudinal treatment studies. The latter suggestion has been made by Olichney (2013) and through the years, changes in the amplitude, latency and topographical distribution of the N400(-effect) have been described as "markers of response to therapeutic efforts" by multiple authors (Aerts, Batens, et al., 2015; Wilson et al., 2012). For the electrophysiological monitoring of language recovery, the availability of normative data will facilitate an accurate interpretation of semantic ERPs by distinguishing pathological effects from healthy ageing effects, for both men and women. Ideally, the obtained ERP results are integrated with findings from the behavioural language tests in order to determine the therapeutic strategy (Cocquyt et al., 2020a). As such, it is beneficial that two distinct ERP tasks were developed since both categorical and associative relationships are targeted in logopedic diagnostics (Visch-Brink et al., 2005; Visch-Brink et al., 2010) and are frequently used as therapeutic cueing strategies (Lowell et al., 1995; Saito & Takeda, 2001). Importantly, the clinical value of the N400 (effect) and the associated normative data applies to patients with aphasia due to acute (Cocquyt et al., 2020a; Cocquyt et al., 2020b) or degenerative brain damage (Stalpaert et al., 2020), but undoubtedly to other neurological populations as well (Angwin et al., 2017; Boyd et al., 2014; Olichney & Hillert, 2004; Olichney et al., 2002; Olichney et al., 2008).

5. Conclusion

The current study provides evidence that the processing of categorical and associative relationships between auditorily presented words is subjective to both healthy ageing and gender effects. With increasing age, enhanced amplitudes of the early P1 component and delayed onsets of the N1 and P2 were observed, possibly associated with changes in neural inhibition and altered neural recovery cycles respectively. For both types of semantic relationships, healthy ageing did not significantly modulate the size (amplitude) or the onset (latency) of the main N400 effect, which supports the view that the integrity of semantic knowledge is relatively stable along the life trajectory. Topographical changes were observed for associative relationships only, as reflected by an increased right-hemispheric lateralisation pattern from middle-age on, that could be compensatory in nature. Gender-related differences were found as women showed larger P2 amplitudes and larger semantic priming effects in comparison to men. The latter findings suggest a deeper level of (lexico-)semantic word processing in women. Finally, the developed normative electrophysiological data will be useful in clinical populations with acquired language disorders as well as for scientific purposes.

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Declaration of competing interest

No conflicts of interest were reported by the authors.

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