

EQUIVALENCE OF DIFFERENT LANGUAGE VERSIONS OF THE INTERNATIONAL SHOPPING LIST TEST IN THE PHASE 3 MISSION AD STUDIES

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Introduction

- The Eisai Phase 3 MissionAD studies assess the effects of the BACE inhibitor elenbecestat on clinical and biomarker outcomes in early Alzheimer's Disease (AD).
- Entry into these studies requires impairment on the immediate or delayed recall components of the International Shopping List Test (ISLT).
- The ISLT is a supervisor administered verbal list learning test where individuals learn a list of 12 food items. Verbal list learning tests are commonly used as measures of verbal episodic memory given, in the context of early AD, impairment manifests in fewer total words being recalled both during the immediate learning rounds and following a delay¹.
- The ISLT was developed specifically for use across different cultural backgrounds and to-date, has been translated into over 90 countries, with new cultures and language groups being continually added to the library of available languages.
- The ISLT has been validated in over 90 countries, and across both mild cognitive impairment (MCI) and AD^{1,2}. Studies report high levels of stability and consistency when comparing groups of diverse languages. Specifically, equivalent magnitudes of impairment and rates of change over 12 months has been reported across cultures³.
- With the increase in Phase 3 trials, study teams require measures appropriate for initial screening that can be used in global trials. The Phase 3 MissionAD studies are currently assessing patients on the ISLT in 29 countries, and thus these data provide an opportunity for further exploration of the cross-cultural validity of this measure.
- This aim of this study was to determine the equivalence of performance characteristics between different language versions of the ISLT in the large, global MissionAD studies.

Methods

- Clinical sites identified subjects for potential entry into the elenbecestat studies based on their likelihood of meeting criteria for early AD (MMSE \geq 24; CDR-GS=0.5; CDR Memory \geq 0.5).
- Following consent, the ISLT immediate and delayed recall trials were administered. The ISLT requires 5 minutes to complete and contains three immediate recall trials (36 words in total) and one delayed recall trial (12 words in total). The ISLT yields two performance measures: total words correct for immediate recall and delayed recall.

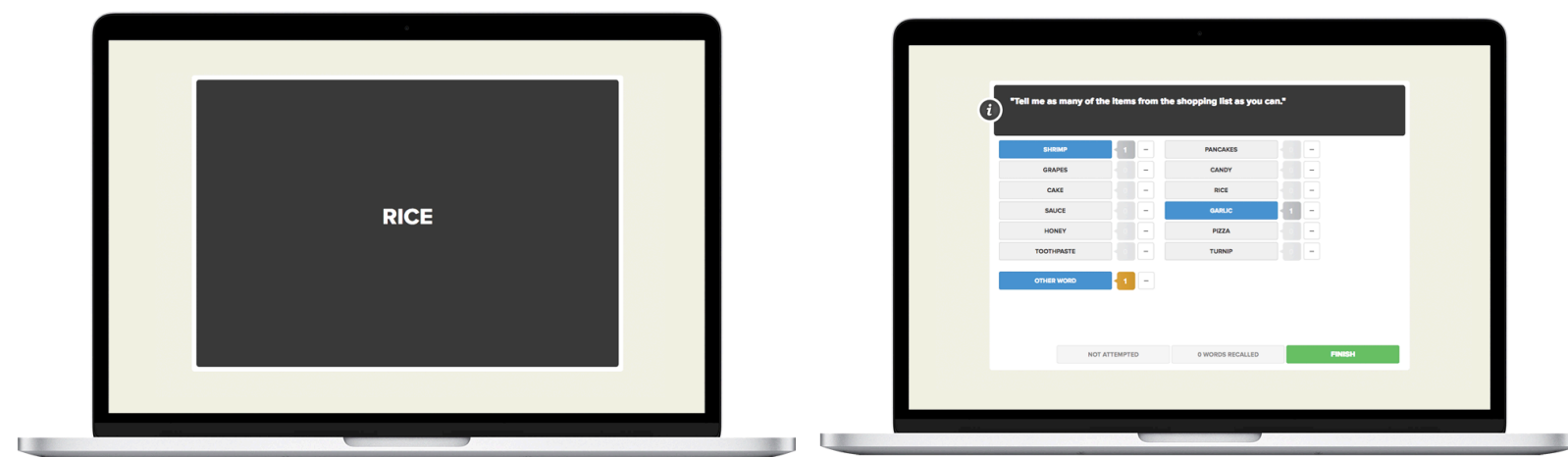


Figure 1. Example stimuli from the International Shopping List Test (ISLT).

- Normative data is available for the ISLT, and both the immediate and delayed recall trials are scored automatically using Cogstate's secure data processing sever.
- Only subjects classified as impaired (z-score \leq -1.0) on either the ISLT immediate or delayed recall were included.
- Language versions with N>100 were included to provide sufficient power, yielding 13 languages across 12 countries at the time of the analysis (see Table 1).

Data Analysis

- Descriptive statistics were computed for individual trials, the ISLT immediate and delayed recall across the language groups. Primacy and recency scores, serial position curves, and inter-trial correlations were also evaluated.

Methods

Table 1. Languages and associated sample sizes for the analysis sample.

Language	Language Abbreviation	N	Percentage
Czech (Czech Republic)	cz_CR	165	3.0%
German (Germany)	ge_GE	106	1.9%
English (Australia)	en_AU	114	2.1%
English (Canada)	en_CA	109	2.0%
English (Great Britain)	en_GB	521	9.4%
English (USA)	en_US	1811	32.8%
Spanish (Argentina)	sp_AR	148	2.7%
Spanish (Spain)	sp_SP	200	3.6%
Spanish (USA)	sp_US	1059	19.2%
Japanese (Japan)	ja_JP	673	12.2%
Korean (South Korea)	ko_KR	167	3.0%
Polish (Poland)	pl_PL	315	5.7%
Slovak (Slovakia)	sk_SK	140	2.5%
Total	Total	5528	100.0%

Results

Sample

- Data for 8,711 consented subjects in 35 languages had been collected at the time of the analysis.
- Of these 35 languages, 13 languages across 12 countries had a sample of N>100. Limiting the sample to these languages and countries yielded a final sample of 5,528 subjects (mean age=71.21, SD=7.91, range 43 to 86, 51.5% female).

ISLT Learning Trajectory

- In all 13 language versions of the ISLT, performance improved across Trials 1 to 3 (see Figure 2). This trajectory reflects the expected learning curve, with consistency in words recalled at each learning trial evident across language groups.
- A moderate decay in performance occurred between Trial 3 and the Delayed Recall trial. Total words recalled during the Delayed Recall trial was lower than total words recalled during the first learning trial for several language groups.

Results

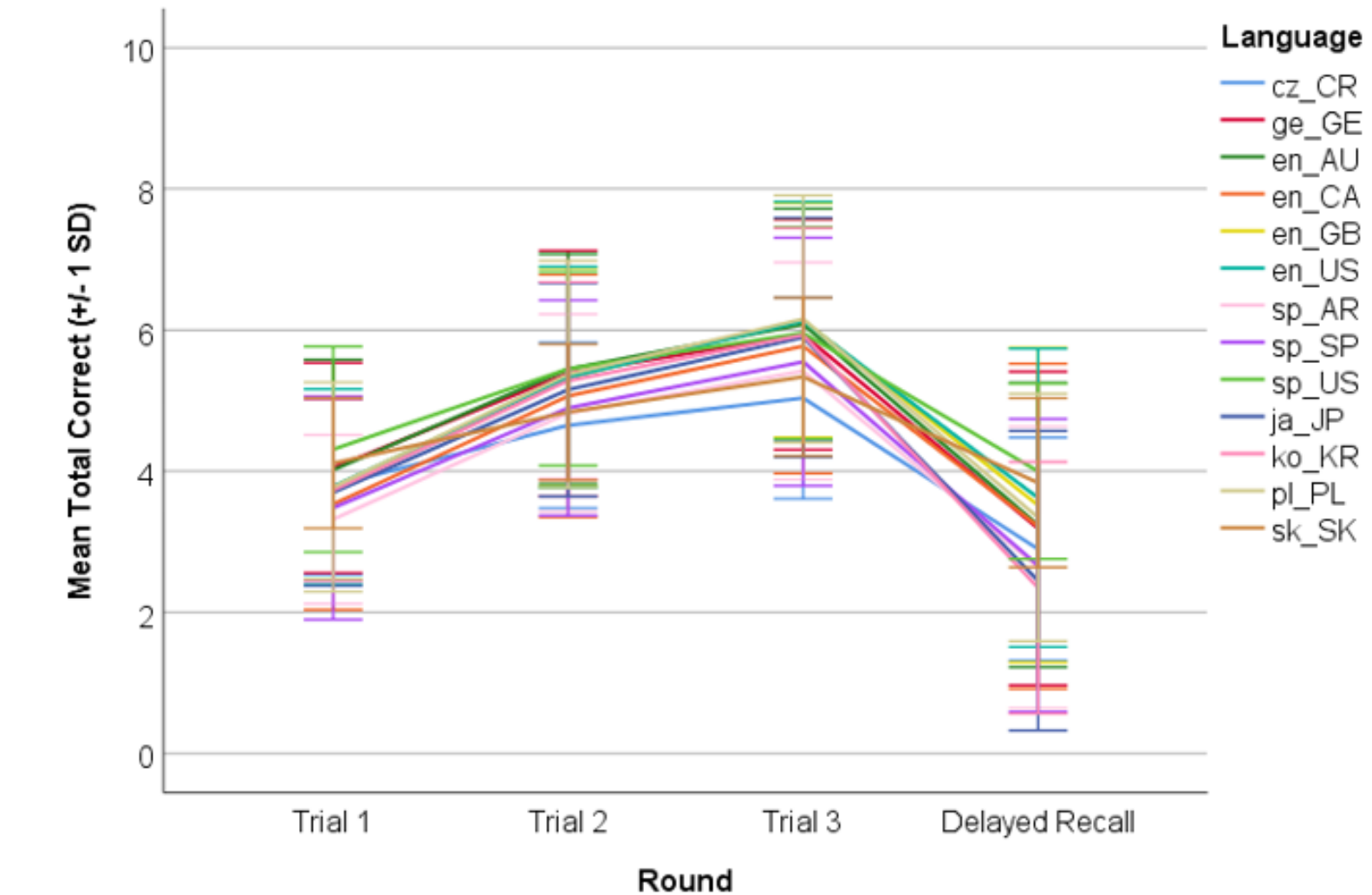


Figure 2. Performance on Trials 1, 2 and 3 and Delayed Recall on the ISLT for each language.

Inter-Trial Correlations

- The magnitude of inter-correlations on the ISLT was highest between Trials 1 and 2 and lowest between Trial 1 and Delayed Recall, indicating that the strength of relation was highest between trials of closest proximity.

Table 2. Inter-trial correlations for the ISLT Learning and Delayed Recall trials.

Trial	Trial 1	Trial 2	Trial 3	Delayed
Trial 1	–	.55**	.44**	.29**
Trial 2	–	–	.65**	.40**
Trial 3	–	–	–	.47**
Delayed	–	–	–	–

** $p < .001$

Primacy and Recency Effects

- Primacy and recency effects were evident on serial position curves for all languages, with words at the beginning and end of the 12-item list most frequently recalled, whilst words in the middle were most frequently omitted.

Results

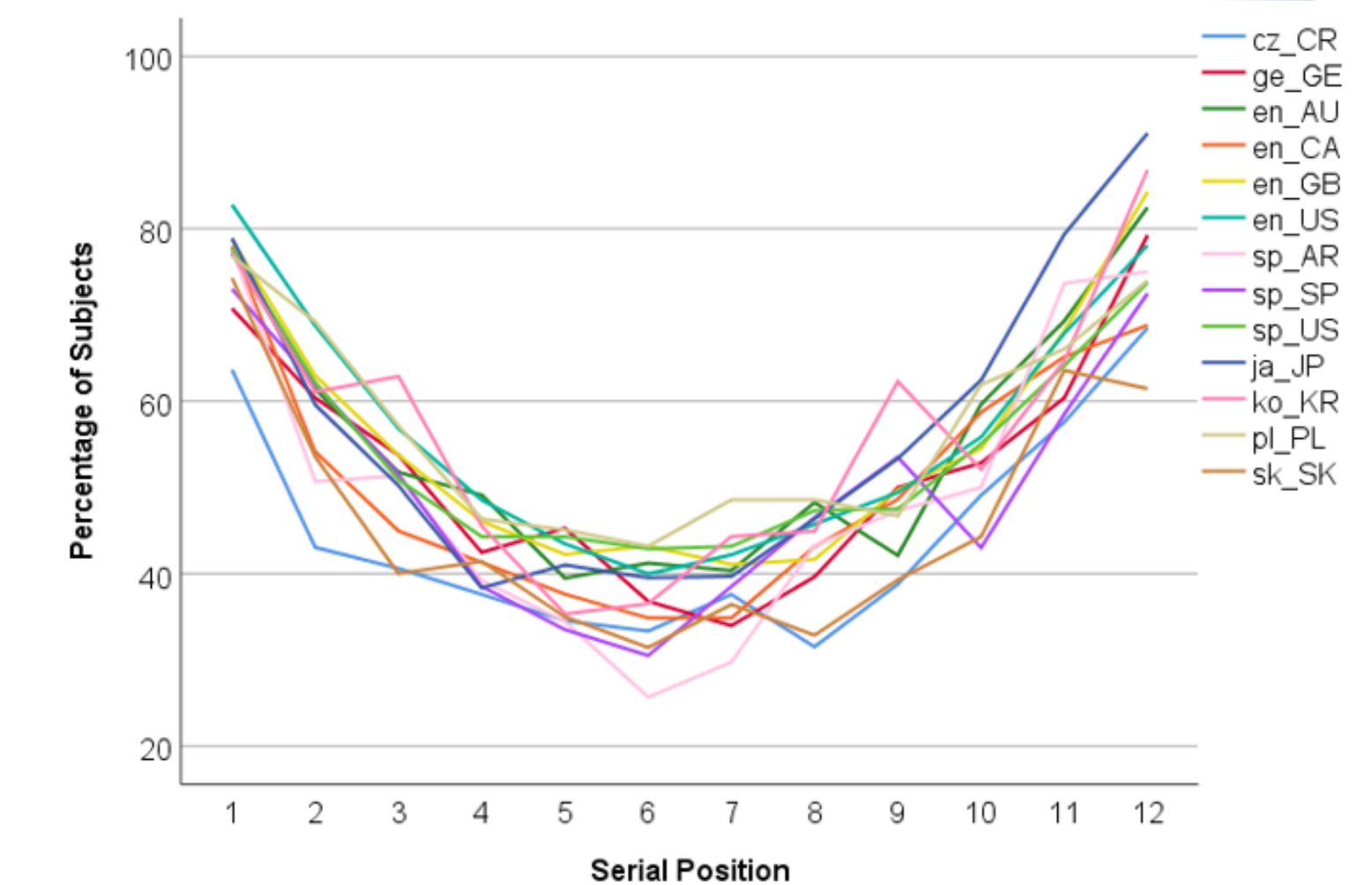


Figure 3. Serial position curve for each language on Trial 3 of the ISLT.

Conclusions

- Different language versions of the ISLT provided equivalent performance in learning trajectory and memory decay following a delay in a globally represented sample of older adults with memory impairment seeking entry to the MissionAD program.
- These findings provide evidence for the cross-cultural utility of the ISLT.

Acknowledgments

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Disclosures

Bruce Alcala and Michelle Gee are full-time employees of Eisai Incorporated and Eisai Limited respectively. Paul Maruff and Adrian Schembri are full-time employees of Cogstate Incorporated.

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