

Harmonizing Cognitive Tests of Episodic Memory and Executive Function Across Randomized Controlled Trials

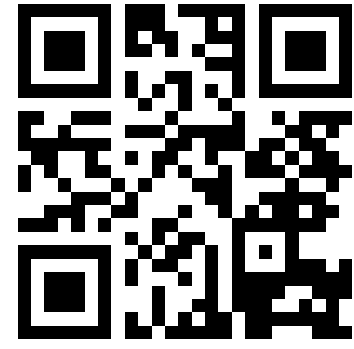
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InLife Study

- Pool and harmonize participant-level data from U.S. randomized controlled trials with lifestyle behavior interventions promoting:
 - Physical, cognitive, social activities, and/or healthy diet
 - Aimed at improving long term cognition in older adults
- The InLife Study aims to quantify the impact of changes in lifestyle health behaviors on cognitive outcomes, including:
 - Episodic Memory** – ability to encode and store, then consciously retrieve information about specific events at particular times and/or places
 - Executive Function** – conceptualized as having four components: volition, planning, purposive action, and effective performance

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Methods

- Group of experts in cognitive aging, psychology, statistics, and psychometrics meeting regularly since 2025
- Collecting, categorizing, and combining cognitive tests across trials with a harmonization process (see middle column →) that:
 - Is reproducible — well-documented steps with decisions tracked and approved as a group
 - Preserves the relationships between cognition and lifestyle that will be the subject of future analyses

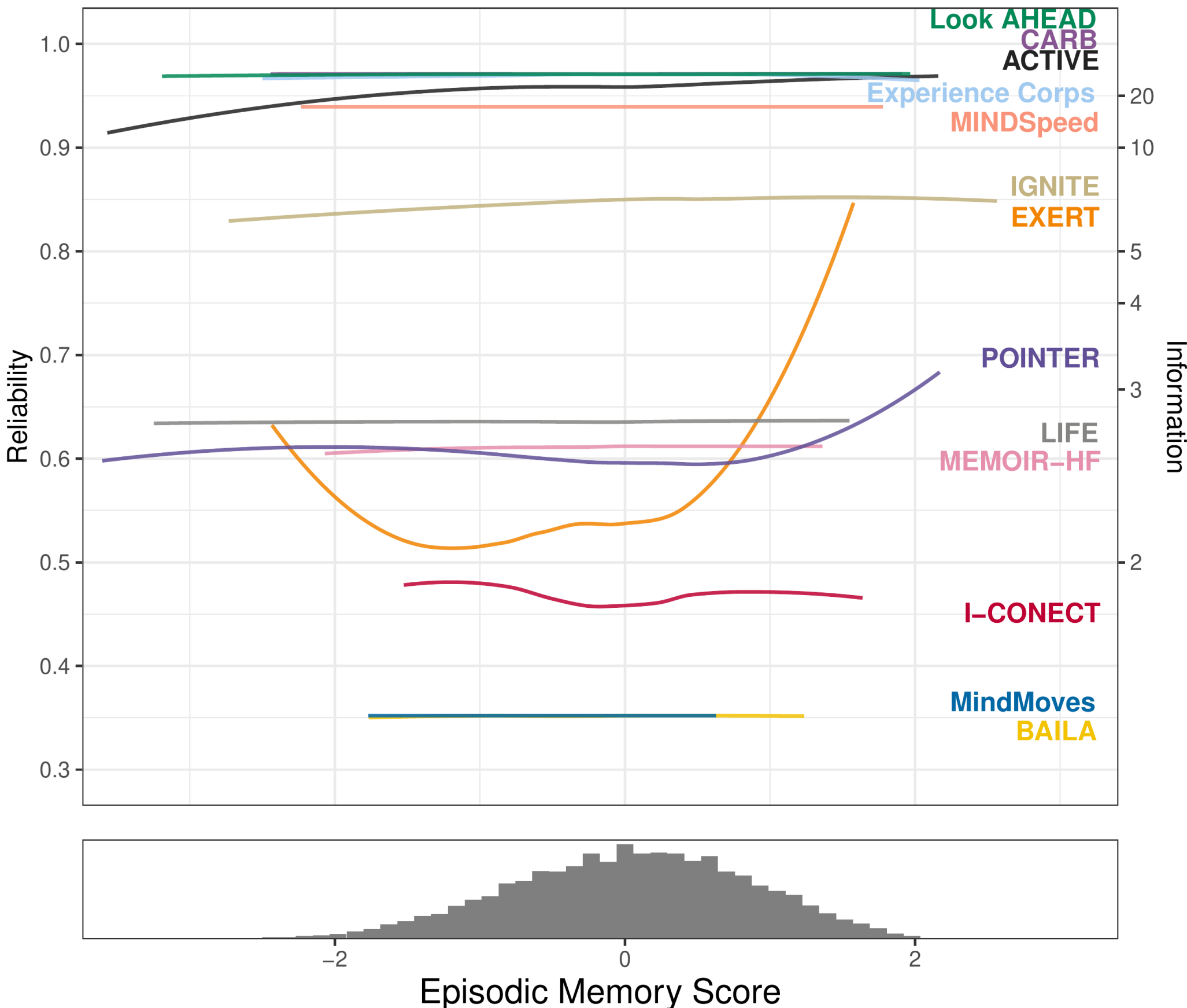
Table 1: Availability of cognitive tests by domain across 13 randomized controlled trials

Episodic Memory		Executive Function (including Working Memory)	
Test Name or Type	RCTs	Test Name or Type	RCTs
Story Recall	7	Trail-Making Test	10
Auditory Verbal Learning Test	6	Digit Symbol Substitution Test	8
Hopkins Verbal Learning Test	4	Stroop*	7
Cogstate C3 Battery	2	Digit Span Test	5
Figure Recall Tests	3	NIH Toolbox	4
Other Unique Tests	2	Cogstate One-Back	2
		Task Switching	2
		Other Unique Tests	5

Some similar tests (e.g. digit symbol substitution and digit modalities) are grouped together under a single test name.

*Stroop is not considered a shared test across studies due to differing protocols

Figure 1: Reliability and information curves for Episodic Memory by study and a histogram of all scores across studies



The combined InLife dataset now contains harmonized **Episodic Memory and Executive Function** scores on common scales across 13 randomized controlled trials for 11,304 participants and for each of their attended visits.

InLife Cognitive Harmonization Process

- 1 Categorize the cognitive tests from each study into the EM and EF domains
- 2 Decide which test outcomes are shared across studies by comparing administration and scoring protocols
- 3 Initial data exploration (outliers, missing values, distributions), cleaning, and combining of test results from all studies into the same dataset
- 4 Within-study Confirmatory Factor Analysis (CFA) models — using model fits to verify within-study consistency of test outcomes with a single factor (EM or EF)
- 5 Step-wise CFA model fitting to produce an overall EM or EF score on the same scale for every participant at each of their attended visits across all studies.

Table 2: Modeling steps to produce an Episodic Memory score for a combined dataset of participants and visits from all studies.

CFA Model	Model Data	Story Recall	Cogstate C3 Tests	AVLT	HVLT	Other
1	POINTER	X	X			SRT
2	EXERT	X	X	X		
3	ACTIVE	X		X	X	
4	IGNITE	X			X	BVMT, VPA, RISE
5	I-CONNECT	X			X	Benson Figure
6	LIFE	X			X	Rey-O Figure
7	All 13 RCTs	X	X	X	X	All of the Above

Parameters for test outcomes estimated in model fit

Parameters fixed to estimates from previous fit

Table 3: Summary statistics (mean ± standard deviation across all available visits) of Episodic Memory and Executive Functioning scores by study.

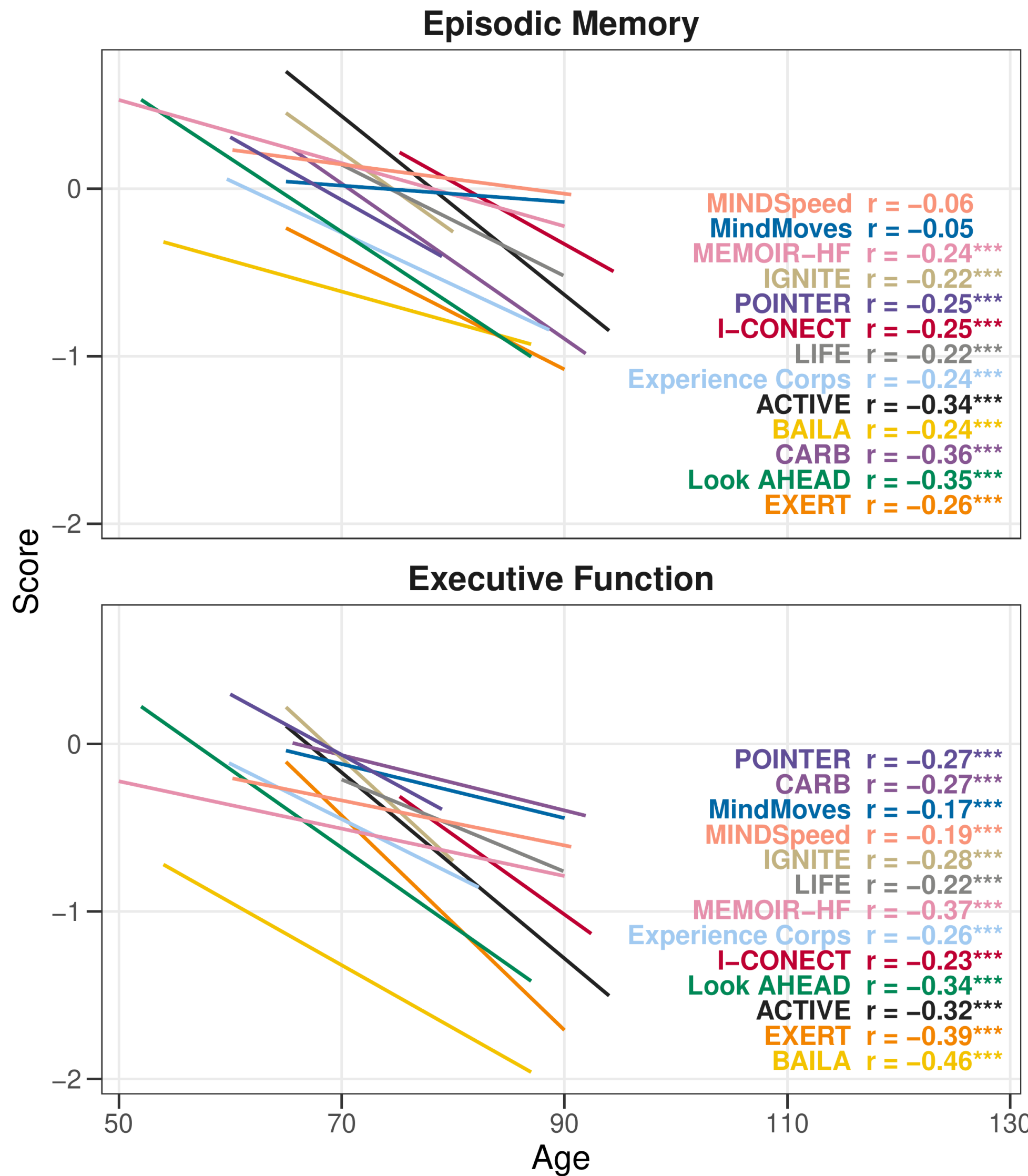
Study	PubMed ID	Participants	Age	EM Score	EF Score
ACTIVE	24417410	2,629	73.6 ± 5.9	0.26 ± 0.90	-0.35 ± 0.98
BAILA	35445687	259	65.0 ± 7.4	-0.52 ± 0.57	-1.13 ± 0.61
CARB	37268243	182	75.7 ± 6.5	-0.23 ± 0.84	-0.16 ± 0.40
EXERT	40271887	274	74.7 ± 6.0	-0.55 ± 0.78	-0.72 ± 0.97
Experience Corps	19139252	606	67.3 ± 5.9	-0.18 ± 0.75	-0.36 ± 0.76
I-CONNECT	37935416	186	81.1 ± 4.6	-0.00 ± 0.67	-0.59 ± 0.93
IGNITE	31465859	578	69.8 ± 3.8	0.22 ± 0.79	-0.08 ± 0.82
LIFE	24866862	1,388	78.9 ± 5.2	-0.15 ± 0.78	-0.45 ± 0.65
Look AHEAD	28067945	2,622	68.9 ± 5.5	-0.16 ± 0.78	-0.52 ± 0.85
MEMOIR-HF	34763080	220	69.2 ± 8.7	0.17 ± 0.67	-0.49 ± 0.33
MindMoves	40442881	233	72.8 ± 5.8	0.00 ± 0.54	-0.16 ± 0.55
MINDSpeed	40511694	158	66.0 ± 5.7	0.18 ± 0.84	-0.28 ± 0.41
POINTER	40720610	1,992	68.2 ± 5.1	0.00 ± 0.77	0.00 ± 0.69

*Primary reference for each study can be accessed by replacing *ID* with the number from the table above in this url: <https://pubmed.ncbi.nlm.nih.gov/ID/>

Results

- EM and EF scores each on a common standardized metric (mean = 0, SD = 1 across all trials) for ~42,000 total observed attended visits of 11,304 participants (Table 1)
- Reliability of EM scores is above 0.80 in 6 of 13 trials and at or above 0.60 in 9 of 13 (Figure 1).
- EF and EM scores exhibit expected relationships with age (significant negative correlations; Figure 2)

Figure 2: Linear trends of Episodic Memory and Executive Functioning scores with age, grouped by study and including correlation (r) estimates and significance (*=p<0.05, **=p<0.01, ***=p<0.001).



Conclusion

- The InLife study now has two harmonized cognitive outcomes (EM and EF) available for pooled analyses across 13 RCTs
- These harmonized scores:
 - Recover expected age relationships
 - Behave consistently across trials
- Are products of a reproducible harmonization process applicable to further cognitive outcomes and trials.

Next Steps

- The InLife team will take additional steps validate the harmonized EM and EF scores with:
 - More external comparisons (education, sex, etc.)
 - Checking for biases or other fit issues (e.g. differential item functioning)
- The same harmonization process will be applied to the study's secondary cognitive outcomes: processing speed and global cognition
- Harmonized EM and EF scores will serve as main outcomes for the central analyses of the InLife study

Acknowledgements

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