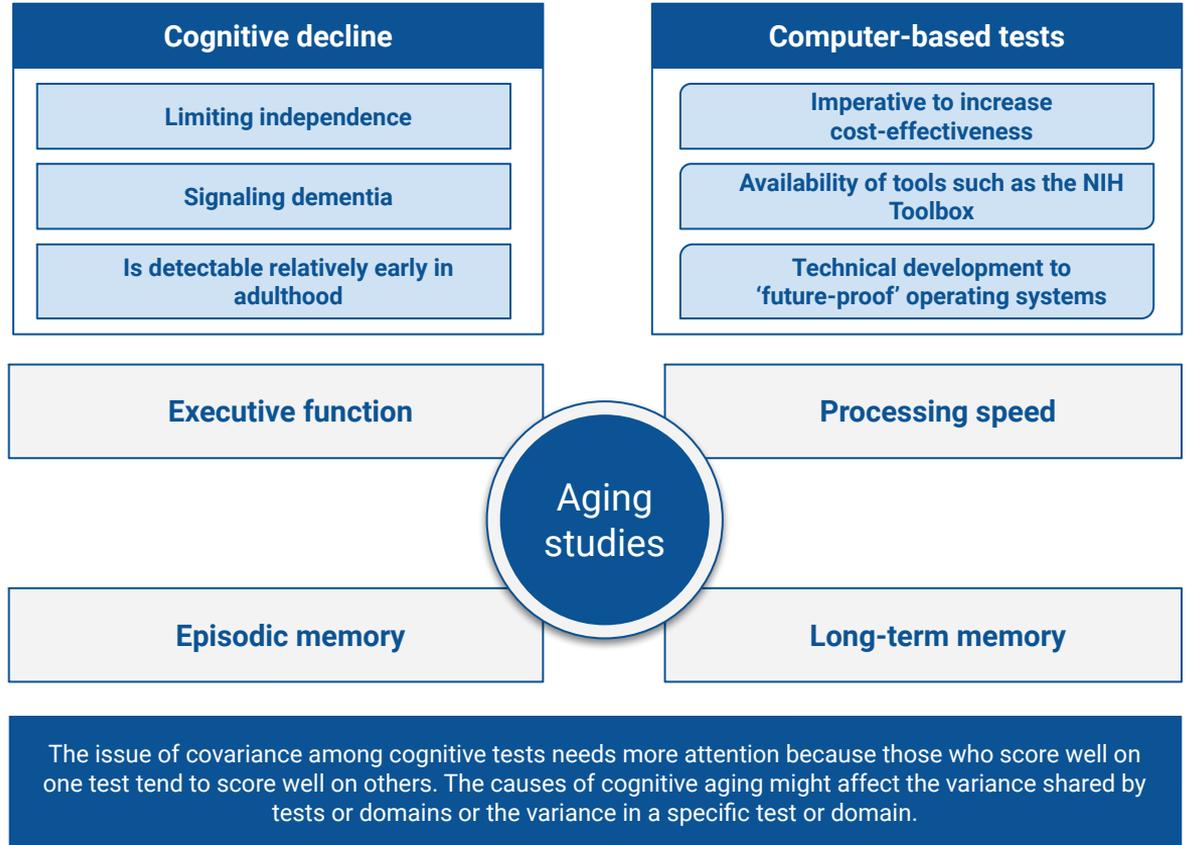


Neurological/Cognitive Biomarkers



Cognitive Biomarkers Overview

Cognitive decline may limit independence and signal dementia, and, although debated, evidence indicates that the onset of cognitive decline is detectable relatively early in adulthood, for example from around 45 years of age or earlier in some functions. Executive function, processing speed and episodic memory – are a possible minimum set of domains to be assessed in aging studies. If assessment time allows, tests of crystallised cognitive ability and non-verbal reasoning would be useful additions. Executive function is markedly affected by aging, exhibiting an inverted U-shape pattern across the lifespan. Processing speed declines progressively with age and is associated with greater mortality risk, cardiovascular and respiratory diseases. In addition, episodic memory is sensitive to brain aging and declines in individuals with mild cognitive impairment and neurodegenerative diseases. A standard deviation advantage in memory is associated with 21 % reduction in mortality risk among older individuals.



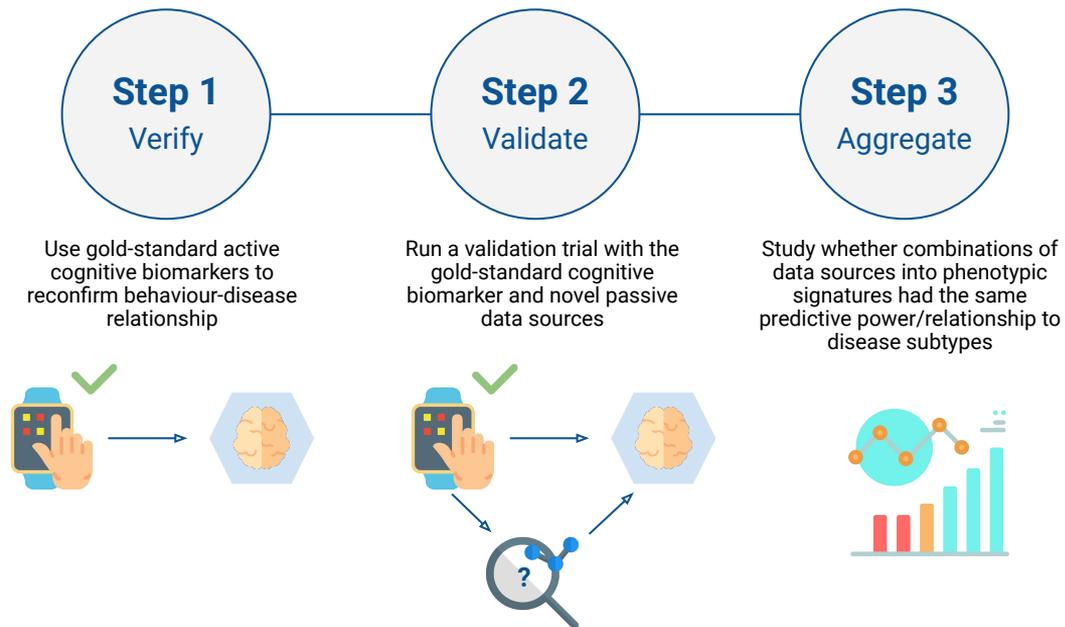
Cognitive Biomarkers Weaknesses

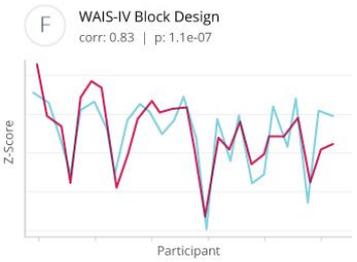
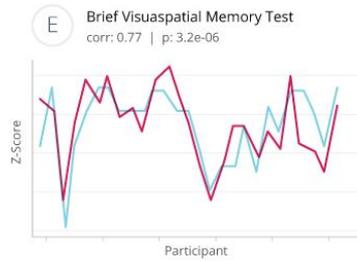
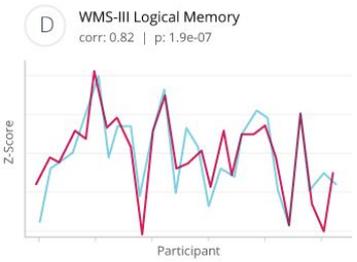
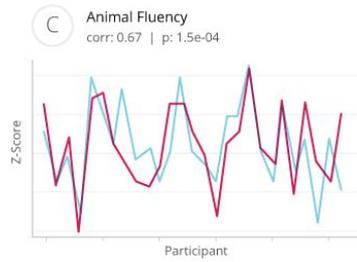
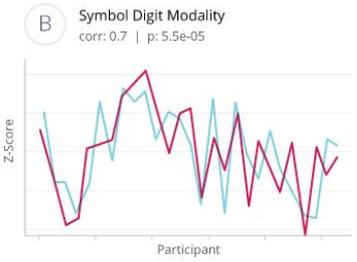
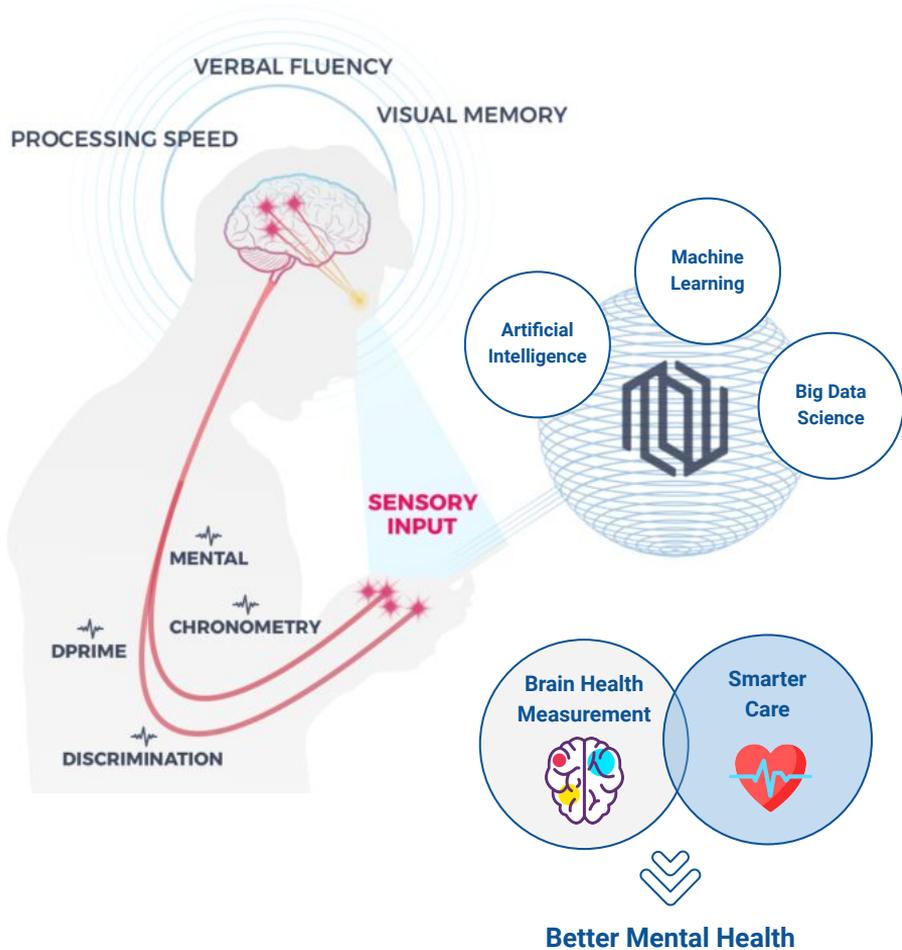
To date, computer-based tests are not widely used in major cohorts; availability of tools such as the NIH Toolbox and the imperative to increase cost-effectiveness are likely to drive the migration to digital methodologies. This will require that tests are supported by ongoing technical development to 'future-proof' operating systems and hardware. Where tests are administered repeatedly in the same individuals problems associated with practice and familiarity need to be addressed. The issue of covariance among cognitive tests needs more attention because those who score well on one test tend to score well on others. Timothy A. Salthouse and others have highlighted that the causes of cognitive aging might affect the variance shared by tests or domains or the variance in a specific test or domain.

Passive biomarkers are a hot topic at the moment with the rise of digital phenotyping and the prospect of being able to monitor a person's health status non-invasively without the participant having to engage in specific tasks. To facilitate these passive biomarkers, large datasets are required with extensive validation in healthy and clinical populations.

Passive data sources can be combined to create complex phenotypic signatures or digital avatars which relate to a person's health or disease status. These can be enhanced by coupling passive data sources with active cognitive assessments to determine relationships with health.

Active cognitive biomarkers serve as both the immediate gold-standard endpoints for cognitive function, but also as the benchmark for training and validating novel passive measurements against.

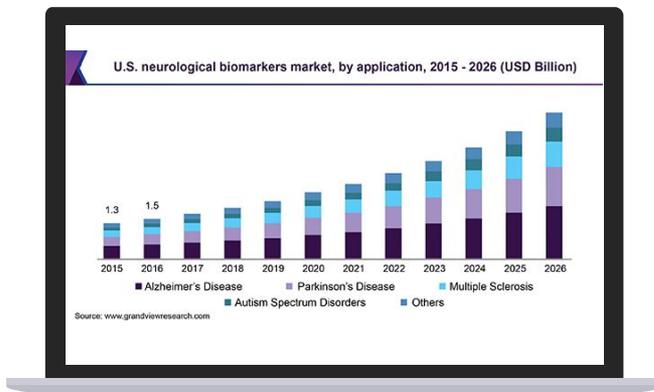




— Test Score
— Digital Biomarker

Neurological Biomarkers: Overview

The global neurological biomarkers market size was estimated at USD 5,564.8 million in 2018 and is expected to exhibit a CAGR of 14.5% during the forecast period. Rising prevalence of neurological diseases and increasing emphasis on early diagnosis & treatment are expected to drive the market growth.



ExAtlas: Gene Expression Meta-analysis

Description of ExAtlas

ExAtlas is a tool for meta-analysis of gene expression data. On this server, the download of raw data is no longer supported. Thus we recommend switching to the mirror server at Rice University (131.113.175.206/exatlas). In contrast to other software, it compares multi-component data sets and generates results for all combinations (e.g., all gene expression profiles vs. all GO annotations). Main functions are: (1) standard meta-analysis (fixed and random effects), (2) Fisher's method analysis of (3) global correlations between gene expression data sets, (4) gene set enrichment, (5) gene set overlap, (6) gene association (Expected Proportion of False Positives, EPPF), (7) statistical analysis of gene expression (ANOVA, PCA, FDR). Results are presented graphically as heatmaps, bar-charts, or 3-D images (PCA). Gene expression data is centered automatically from GEO/NCBI database. Several most popular public data sets (e.g., GNF, Gene Ontology, KEGG, GAD phenotypes) are pre-loaded and can be used for functional annotation. HELP: A guide to ExAtlas.

NOTE: The error message "Operation failed!" means a suspicious command or data. Please send a message to admin@exatlas.org and explain the problem.

[START USING EXATLAS \(as guest\)](#)

To get an account, [register here](#) (free).
You can also log in as "guest" to have full functionality in our session.
The advantage of [registration](#) is that you can keep your data and results on the server.

Login to ExAtlas:
User login:
Password:

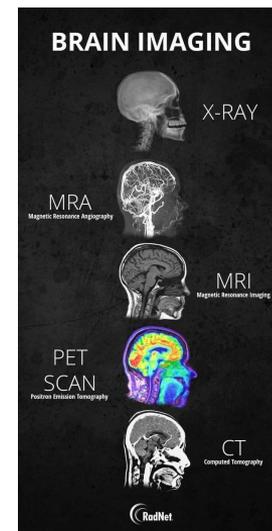
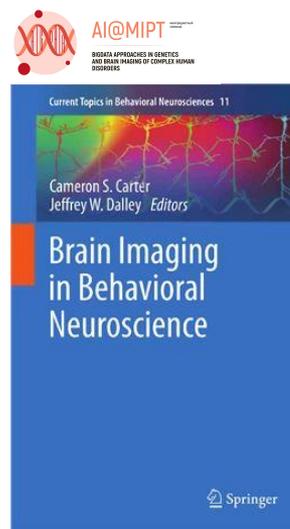
How to cite ExAtlas: Shao, A.A., Schlesinger, D., and Ko, M.S.H. 2015. ExAtlas: An interactive online tool for meta-analysis of gene expression data. *J. Bioinform. Comput. Biol.* DOI: [10.1142/S1747020815500095](https://doi.org/10.1142/S1747020815500095)

Please report any problems to admin@exatlas.org.

Biomarkers

Executive Function, Verbal Fluency, Processing Speed, Digit-Symbol Coding, Working Memory, Digit Span Backward, Crystallized Ability, Boston Naming Test, Attention. Stroop Task, Non-Verbal Reasoning, Raven's Progressive Matrices, Visual Memory and Visuospatial Ability, Benton Visual Retention Test and Block Design Test, Verbal Memory & Learning Rey, Auditory Verbal Learning Test

fMRI, brain imaging analysis The Virtual Brain (TVB)



Brain imaging refers to the usually non-invasive or minimally invasive techniques that enable imaging the structure or function of the brain. Brain imaging techniques take advantage of X-rays, radioactive labelling, magnetic fields induced by the brain's electrical activity, or optical absorption or paramagnetic properties of haemoglobin.

Neurological Biomarkers: SWOT Analysis



S

Strengths

- Good support: test is widely used by clinicians and researchers, and also used extensively to aid in the selection of employees for jobs that require fine and gross motor dexterity and coordination; due to this, there is a considerable amount of research available in support of its use in clinical practice and scientific research.
- Strong reliability as aging marker. There are a number of studies that provide age-valued norms.
- Good operability. Low complexity level. No special training is required for use and interpretation, although it is recommended. The manual provides detailed directions, scoring, and referenced norms across the lifespan.
- Good inter-patient adaptability. The ranges are optimally standardized; thus, it can be used in a wide variety of patient populations where dexterity is of concern.
- Good transferability. The mental tests would have a similar value in a variety of different health-related implementations, including measurements of functional age in panels.



O

Opportunities

- Identifying the biological correlates of late life cognitive function is important for developing treatments to help reduce, age-related cognitive decline.
- To develop a low-cost, modular touch screen device for integrating multiple cognitive & biometric assessment technologies.
- To develop statistical models and functional age calculation algorithms.



W

Weaknesses

- Studies have suggested that group administration may lead to increased competitiveness and knowledge of scores can create a situation where subjects try to beat previous scores, thus relativizing the results.
- No fully integrated approach that can easily collect a variety of different data points from human participants.



T

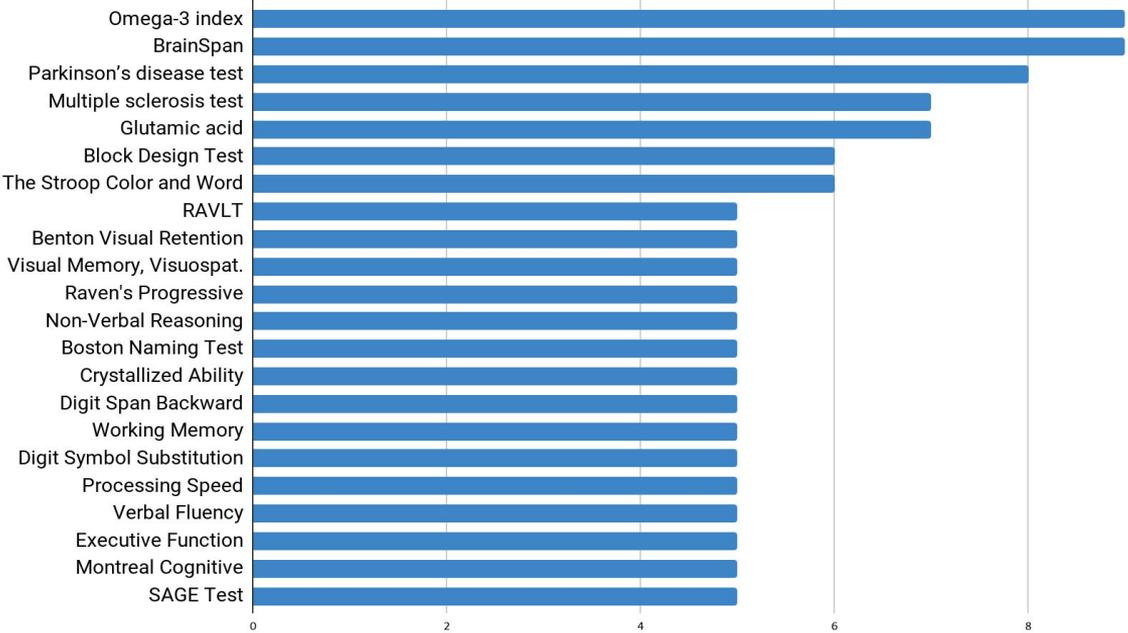
Threats

- Expensiveness and complexity of MRI analysis
- Non accurate writing tests

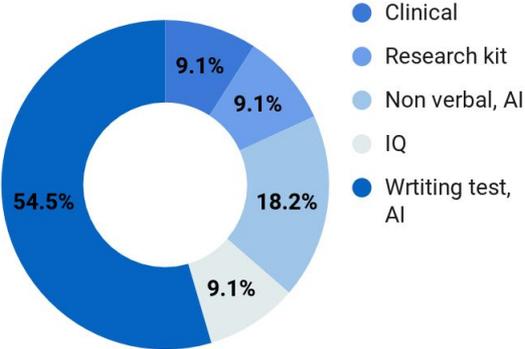
Neurological Biomarkers: TRL Analysis

TRL average = 6.52

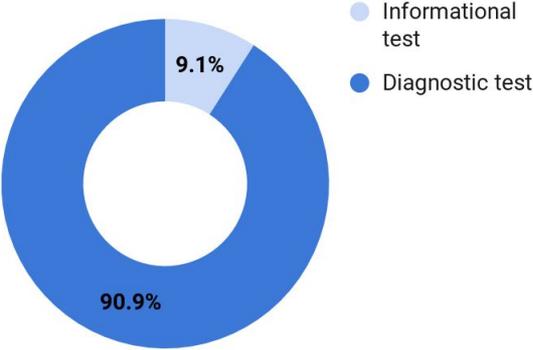
TRL for Neurological Biomarkers



Conditional Stage



Approved for



Neurological Biomarkers: Commercial Examples

Olink Proteomics (Sweden, United States): Olink offers an unmatched high-multiplex technique to identify actionable biomarkers, with a strong focus on the human plasma proteome. **Products/Services:** Medical test. Biotechnology, Health Care.



Myriad RBM, Inc.(United States): Myriad RBM, Inc. is the multiplexed immunoassay testing laboratory that solves complex drug development challenges with innovative biomarker services and a novel whole blood immunophenotyping device (TruCulture®). **Products/Services:** Medical test. Biotechnology, Health Care.



BEYOND VERBAL (Israel): Uses Voice and AI to extract human emotions and reveal Vocal Biomarkers – acoustic features indicating various health conditions. In collaboration with leading medical institutions, Beyond Verbal performs multiple clinical trials and conducts BIG DATA projects aimed at revealing signs of cardiovascular, pulmonary, neurological and other diseases and chronic medical conditions in the voice – allowing continuous patient monitoring and predictive analytics. **Products/Services:** Vocalis Health platform. Research Use Only. Pilot, validation. Analytics, Artificial Intelligence, Big Data, Call Center, Cloud Computing, Health Care, Internet of Things, Machine Learning, Market Research, Medical, Mobile, Personal Health, Wellness.



COMPANION MX (United States): A digital health technology company with a proven platform for proactive mobile mental health monitoring for better clinical outcomes. Born out of the Massachusetts Institute of Technology Media Lab and clinically validated at Harvard Medical School teaching hospitals and multiple Veterans Affairs clinics, the Companion™ system uses active monitoring of voice and passive monitoring of other smartphone metadata to continuously produce acoustic and behavioral biomarkers that predict core symptoms of mood and anxiety disorders. **Products/Services:** Companion™ mental health monitoring system, AI Platform. Clinically validated, Mobile, health care.



Neurological Biomarkers: Publication Overview

