

Current standards of neuropsychological assessment in epilepsy surgery centers across Europe

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SUMMARY

We explored the current practice with respect to the neuropsychological assessment of surgical epilepsy patients in European epilepsy centers, with the aim of harmonizing and establishing common standards. Twenty-six epilepsy centers and members of “E-PILEPSY” (a European pilot network of reference centers in refractory epilepsy and epilepsy surgery), were asked to report the status of neuropsychological assessment in adults and children via two different surveys. There was a consensus among these centers regarding the role of neuropsychology in the presurgical workup. Strong agreement was found on indications (localization, epileptic dysfunctions, adverse drugs effects, and postoperative monitoring) and the domains to be evaluated (memory, attention, executive functions, language, visuospatial skills, intelligence, depression, anxiety, and quality of life). Although 186 different tests are in use throughout these European centers, a core group of tests reflecting a moderate level of agreement could be discerned. Variability exists with regard to indications, protocols, and paradigms for the assessment of hemispheric language dominance. For the tests in use, little published evidence of clinical validity in epilepsy was provided. Participants in the survey reported a need for improvement concerning the validity of the tests, tools for the assessment of everyday functioning and accelerated forgetting, national norms, and test co-normalization. Based on the present survey, we documented a consensus regarding the indications and principles of neuropsychological testing. Despite the variety of tests in use, the survey indicated that there may be a core set of tests chosen based on experience, as well as on published evidence. By combining these findings with the results of an ongoing systematic literature review, we aim for a battery that can be recommended for the use across epilepsy surgical centers in Europe.

KEY WORDS: Epilepsy surgery, Neuropsychology, Diagnostic, Consensus, Europe.



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KEY POINTS

- Basic principles of neuropsychological assessment were highly comparable between 25 different epilepsy surgery centers in Europe
- One hundred eighty-six different tools are in use with moderate agreement depending on the cognitive domain to be assessed
- Published evidence for the use of these tools in epilepsy was indicated only in a few cases
- High variability exists with regard to indications, protocols, and paradigms for the assessment of hemispheric language dominance
- A core set of tests with the highest overlap between the centers was discerned

In January 2014, a European pilot network of 13 reference centers and 15 additional collaborating partners for drug-resistant epilepsy and epilepsy surgery, funded by the European Union in the framework of the Health Program (<http://www.e-epilepsy.eu>) (E-PILEPSY, a European pilot network of reference centres in refractory epilepsy and epilepsy surgery, see <http://www.e-epilepsy.eu>) was established. The primary objective is to improve the quality, accessibility, and consistency of presurgical diagnostic approaches in patients with drug-resistant focal epilepsy across Europe. One aim of this network is to describe the requirements and the structure of epilepsy surgical centers and of current practice in brain imaging, source localization procedures,¹ electroencephalography (EEG) monitoring,² and, the focus of the present report, the neuropsychological

Epilepsy surgery is an elective procedure with the ultimate goal of improving the individual's health-related quality of life through sustained seizure freedom or improvement. In addition, successful epilepsy surgery aims at preservation or even improvement of the patients' functional capabilities, mood, and behavior, thereby improving their socioeconomic opportunities and quality of life. In the context of epilepsy surgery, neuropsychology aims to identify epilepsy-related cognitive impairments and their etiologic attribution to lesions, the active epilepsy, drug treatment, and mood within a neuropsychological developmental framework, which takes age at onset and the brain's capacity for reorganization and compensation into consideration.³

Epilepsy surgery can be associated with cognitive decline. Before surgery, up to 80% of patients already show cognitive impairment in at least one neuropsychological domain.⁴ After temporal lobe resections, the most frequent type of surgery, up to 45% may experience a decline in memory.^{5,6} Furthermore, in terms of complications, surgery can lead to new cognitive deficits or an unexpectedly severe deterioration of cognition, such as disabling memory deficits after temporal lobe surgery.⁷ In children, surgery may even have a positive impact on postsurgical cognitive development.⁸ Surgically caused impairments are especially intolerable in the absence of postsurgical seizure freedom.^{9,10} As such, it is important to individually predict postsurgical deficits to a certain degree. Major predictors of neuropsychological outcome include presurgical test performance, reflecting functional integrity of the resected tissues on the one hand, and reserve capacities of assessment and outcome monitoring in patients with drug-resistant epilepsy.

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nonaffected brain structures on the other hand. Additional predictors are cerebral functional plasticity, seizure control, and the burden of antiepileptic drug treatment.^{6,11–14} Neuropsychological examinations after surgery help to objectively quantify cognitive outcomes, indicate the need for rehabilitative care, and, in terms of quality control, help to optimize treatment outcome of resective epilepsy surgery with minimal cognitive risks.^{6,15}

Apart from cognitive problems, affective problems such as depression and anxiety in adults as well as autism and attention-deficit/hyperactivity disorder (ADHD) in children are frequent.¹⁶ Affective problems are seen in up to 50% of surgical candidates and—similar to cognitive and behavioral problems—in part result from epilepsy and its treatment, and in part may share the same underlying pathophysiology with the epilepsy.¹⁷ They are often underdiagnosed and need to be considered and treated.¹⁸ On a superordinate level, quality of life has been identified as a relevant outcome parameter.¹⁹

The assessment and evaluation of the aforementioned parameters is central in the context of epilepsy surgery. The present survey describes how this is being achieved in different reference centers for epilepsy surgery across Europe. Although the neuropsychology task force of the International League against Epilepsy (ILAE) has recently updated the concepts and principles of neuropsychological assessments in epilepsy,²⁰ detailed information about which tests to use is less easy to obtain. Earlier surveys 23 years,²¹ 11 years,²² and 5 years ago^{23,24} have indicated that there is a wide range of neuropsychological tests used in different epilepsy clinics, not to mention in different countries.²¹ In a review of the theoretical and practical issues related to the role of neuropsychology in epilepsy, we postulated an exemplary evidence-based, question-guided, and modular approach that is not only descriptive, but can also make a difference for patients and their treatment.²⁵ For the purpose of E-PILEPSY, however, such a model needs to incorporate content that is acceptable not only on a national basis^{26,27} but also across different centers in different countries.

Communication of the neuropsychological features of patient groups, and of surgical methods and their outcomes across centers and countries calls for a common language. This requires a harmonization of procedures. These procedures need to meet certain methodological criteria such as age-corrected normative data, standardization for repeated measurement, and sensitivity to the factors causing cognitive impairments in epilepsy.

One central and explicit aim of the E-PILEPSY project is to harmonize best practice in epilepsy surgery and develop guidelines and recommendations based on best available evidence. Given historical and legal reasons but also cultural and linguistic diversities, it is an ambitious undertaking to strive for a European standard. As a first step, the current practice in the E-PILEPSY-associated reference centers needs to be documented. To obtain that information we

conducted a survey among all centers participating in the E-PILEPSY project. The second step, which has already been initiated and which will be dealt with in subsequent publications, is a systematic review of the existing literature in order to discern which instruments may best serve the objectives of neuropsychology in the context of epilepsy surgery. In a third step, a selection of tests will be made that will then require normalization and standardization for repeated measurement in each associated European country. In parallel, work on a common web-based database, which will provide tests, materials, and normative data, is in progress.

METHODS

Two separate surveys were sent out electronically to 26 epilepsy surgery centers of the E-PILEPSY network (21 countries, 19 languages: Salzburg, Austria; Gent, Belgium; Sofia, Bulgaria; Zagreb, Croatia; Prague, Czech Republic; Kuopio, Finland; Lyon, France; Bonn and Kork, Germany; Thessaloniki, Greece; Budapest, Hungary; Milan, Italy; Vilnius, Lithuania; Utrecht, The Netherlands; Oslo, Norway; Bucharest, Romania; Moscow, Russia; Madrid, Spain; Gothenburg, Sweden; Geneva, Switzerland; Istanbul, Turkey; and London, United Kingdom). The first survey focused on neuropsychological testing per se and was—in part—similar to the German inquiry in 2008.²⁸ The focus was on interictal, pre- and postsurgical assessment of patients with epilepsy, not on bedside, ictal testing. The second inquiry was related to the assessment of hemispheric dominance for language functions. The surveys were launched in February 2014 and concluded in June 2015. The first survey consisted of 29 questions addressing the neuropsychological assessment per se. The questions comprised multiple choice answers and/or free text fields and covered the following areas: Availability of epilepsy surgery and of neuropsychological service for adults and children, implementation, organization and capacity of the neuropsychological service, indications for the neuropsychological assessment, consequences for clinical decision making and counseling, psychiatric assessment, as well as detailed descriptions of tests and questionnaires that are in use including published evidence for their use in patients with epilepsy.

The second survey on the assessment of hemispheric dominance for language functions was sent out in August 2014 and concluded in June 2015. This questionnaire comprised 12 items centering on the most common methods (IAT, intracarotid amobarbital test; and fMRI, functional magnetic resonance imaging) and included one question on the general decision process of when and how to assess language dominance.

The surveys were completed by neuropsychologists (n = 14) or neurologists (n = 11), with information provided by the neuropsychologists, since the latter were not official participants in the project.

We excluded our own center (Bonn) concerning response to one item of the survey requesting references to studies supporting the validity of the neuropsychological tools for their use in epilepsy. The reason for this decision was that as coordinator of the survey, we wished to avoid any bias. Many of the tests and questionnaires used in our center have been developed and/or validated by our own investigations.

Descriptive statistics were performed using IBM SPSS 22.

RESULTS

Completed questionnaires were received from 25 reference centers corresponding to a response rate of 96%.

Neuropsychological service

Characteristics of the participating centers are shown in Table 1. Epilepsy surgery is performed in-house in 23 of 25 centers (in two cases, epilepsy patients are referred for surgery to a collaborating clinic after presurgical workup). In-house neuropsychological assessment is available in 23 of 25 of the centers; two centers have external collaborating institutions. In those two centers without in-house neuropsychology, information is obtained from the collaborating institutions offering the neuropsychological service. All but one center regard the neuropsychological assessment as an important and indispensable part of the presurgical diagnostic workup.

Although in six centers the neuropsychological service is focused only on patients with epilepsy, most clinics provide

Table 1. Characteristics of participating centers

	Percentage	N	
Epilepsy surgery program			
Provided in-house	92	23	
Of those, adults only	17	4	
Of those, children only	13	3	
Availability of neuropsychological service			
In-house neuropsychologists	92	23	
Of those, service for adults only	26	6	
Of those, service for children only	17	4	
Payment of neuropsychological service			
Package payment in all cases	36	9	
Package for inpatients, separate payment for outpatients	20	5	
Always separate payment	20	5	
"State payment" (no further explanation)	12	3	
No payment	12	3	
Neuropsychological assessment is performed by			
Qualified psychologists only	76	19	
Qualified psychologists and assistants (e.g., students)	24	6	
Neuropsychological clientele (multiple responses possible)			
Epilepsy patients	25	6	
Neurologic patients	33	8	
Neurosurgical patients	13	3	
Patients with nonepileptic psychogenic seizures	8	2	
Patients with chronic fatigue syndrome	4	1	
Psychiatric patients	4	1	
Neuro-oncologic patients	4	1	
Other, not specified	8	2	
Psychiatric service			
Provided in-house	96	24	
Use of standardized psychiatric diagnostic tools (n = 16 valid answers)	75	12	
Performed by psychiatrists	63	15	
Performed by psychologists and/or psychiatrists	29	7	
Performed both by psychiatrist and/or neurologists	4	1	
Performed by psychologists	4	1	
Neuropsychological capacities	Mean (SD)	Median	Range
No. of professionals	2.5 (1.8)	2	1–7
No. of assistants	1.8 (0.84)	2	1–3
Patients tested per year (all cases)	171 (173)	115	10–750
Presurgical patients tested per year	111 (125)	58	4–480
Duration standard battery	3.11 h (1.98)	2.88	1–10 h
Duration presurgical battery	4.52 h (2.47)	4	1.5–10 h

their services to neurological, neurosurgical, and other patient groups as well. Psychiatric service is provided in 92% of the centers; the evaluation is performed exclusively by psychiatrists (60%), exclusively by psychologists (4%), both by psychologists and/or psychiatrists (28%), or both by psychiatrists and/or neurologists (4%). Standardized inventories for the assessment of depression, anxiety, and other psychiatric symptoms are used by 75% (valid answers $n = 16$). The average time needed for a full presurgical evaluation is 4.5 h, ranging between 1.5 and 10 h.

Neuropsychological assessment

Table 2 shows data on the specifications of the neuropsychological assessments. Indications for neuropsychological assessment included localizing (100%), in all cases presurgical (100%) and all but one centers postsurgical (96%) testing, the evaluation of general cognitive performance (92%), monitoring antiepileptic drug (AED) therapy (68%), testing for transient cognitive impairments (TCI) due to electroencephalographic epileptic discharges (56%), as well as for ictal (20%) and postictal (12%) deficits.

Neuropsychological testing is used for clinical decision making that is, to determine the appropriateness (88%) and the extent of surgery (36%), to optimize AED treatment (32%), and to determine the need for cognitive rehabilitation (32%) or psychiatric treatment (24%). These answers were given in response to an open question, so these data might not be exhaustive and may underrepresent the actual frequencies.

The centers largely agree that memory, language, attention, and executive functions need to be assessed as part of a surgical evaluation. There is also agreement regarding the use of normalized and standardized tests, employing either national or international normative data. Few clinics use their own unpublished norms.

Neuropsychological assessment of pediatric patients is provided in 76% of the centers (Table 1). Of 18 valid answers, the majority of centers use standardized developmental scales or tests for infants and toddlers (Table 3). Of 23 centers offering in-house surgery, 19 (83%) provide a surgical program for children. Of those, 17 provide neuropsychological assessment for children. Two centers provide neuropsychological assessment for children but do not offer in-house surgery at all (1) or not for children (1).

Which test instruments are currently used?

Neuropsychological tests and questionnaires

With a total number of 186 different tests and procedures in use in children and adults, the variation in neuropsychological diagnostics between centers was considerable. Table 4 lists only those tests that are used by at least three centers. Multiple answers were possible for each domain. Tests are listed separately for children and adults. Concerning children, the results showed that development and IQ play an important role. Performance testing is nevertheless

Table 2. Neuropsychology: who, why, what—and what for?

	Percentage	N
Test selection is made by		
Neuropsychologists	80	20
Neuropsychologists and/or neurologists	16	4
Neuropsychologists and speech therapist	4	1
Indications for assessment (multiple responses)		
Presurgical/localizing	100	25
Postsurgical testing	96	24
Cognitive performance level	92	23
Side effects of antiepileptic drugs	68	17
Testing of transient cognitive impairments	56	14
Ictal testing	20	5
Postictal testing	12	3
Consequences of neuropsychological assessment (multiple responses)		
Counseling of the patients for or against surgery	88	22
Determining the extent of surgery	36	9
Change of antiepileptic medication	32	8
Referral to rehabilitation programs	32	8
Referral to psychiatry	24	6
Diagnosis of dementia	20	5
Indication for language lateralization	16	4
Timing of surgery	8	2
Immunomodulatory therapy	4	1
Most important domains to be evaluated (multiple responses)		
Memory	96	21
Language	82	18
Attention	64	14
Executive functions	64	14
Visuospatial functions	46	10
Intelligence	36	8
Behavior and mood	14	3
Motor functions	9	2
Norms in use (multiple responses possible)		
Published national normative data	92	23
Published international normative data	80	20
Published local normative data	32	8
Unpublished local normative data	16	4
Centers providing published evidence for use of tests in epilepsy		
No information provided	56	14
Statement that all tests are evidence based but no references given	20	5
References given	20	5
Sources given for normalization of the tools	52	13
Sources given for validation of the tools	40	10

also an issue in children and adolescents. Table 5 provides the source for justifying the selection of this specific test. References for the tests listed are available in published compendia^{29,30} or the websites of Pearson Assessment (<http://www.pearsonassessment.de/>), publisher Hogrefe (<http://www.testzentrale.de/>) and Psytest (<http://www.psytest.net/>).

For the assessment of *intelligence*, seven different scales were indicated, yet the Wechsler Scales for children and adults was used in all except one center. For adults, either

full (90%) and/or abbreviated versions (15%) are employed. In all three participating German-speaking centers, a vocabulary test is used for assessing crystallized and education-dependent intelligence in adults (Mehrfachwahl-Wortschatz-Intelligenztest, MWT-B). For children, the Wechsler scales for school (60%) or preschool (33%) age are applied.

For *developmental diagnostics*, the most popular scale is the Bayley Scales of Infant Development (33%), whereas some centers use the Denver Developmental Screening test or, to measure adaptive behavior, the Vineland Adaptive Behaviour Scale (VABS) (20% each).

For *nonverbal memory functions*, 10 different tests are in use. The Rey-Osterrieth Complex Figure Test (ROCFT) is used most frequently (55%), followed by only a few centers using the Diagnosticum für Cerebralschädigung (DCS-R) and the Benton Visual Retention Test. As for *verbal memory functions*, among 12 different tests, the Rey Auditory Verbal Learning Test is used most frequently (RAVLT, 40% adults, 20% children), followed by the Logical Memory subtest of the Wechsler Memory Scale (WMS-R) for adults (25%). Complete memory batteries are rarely used (WMS and Recognition Memory Test, RMT).

For children, no consensus of more than two centers was achieved for memory testing. Most frequently used are the DCS-R and the RAVLT (20% each).

Short-term and working memory are tested with the Digit Span and Corsi Block-Tapping test by 70% of the centers for adults. These tests are also popular in children (27% block tapping, 40% digit span).

As for *attentional functions*, the Trail Making Test (TMT) is applied by more than half of the centers for testing visual psychomotor speed and task switching. Other, less frequently used attentional tests in adults are the letter cancellation test D2 (Aufmerksamkeitsbelastungstest) in adults (30%) and the Testbatterie zur Aufmerksamkeitsprüfung (TAP, 15%). *Executive functions* are assessed by the Stroop paradigm (45%) or Wisconsin Card Sorting Test (WCST, 15%). Agreement for children, however, is lower, with only the TMT reaching a consensus of 27%. More popular (33%) is the use of subtests from the Developmental Neuropsychological Assessment (NEPSY), which is also used for memory (two centers), language (two centers), motor (two centers), and visuospatial functions (one center).

Twenty-seven different *language tests* are in use. The majority of centers (75% for adults, but only 33% for children) are using the Boston Naming Test, a word-finding test. Despite some reservations described (obsolete items, items dependent on education), there is no established alternative test so far. In addition, many centers assess phonemic (45%) and/or semantic (40%) fluency for adults, based on tests as FAS (subtest of the Neurosensory Center Comprehensive Examination for Aphasia), COWAT (Controlled Oral Word Association Test), LPS (Leistungsprüfsystem),

and RWT (Regensburger Wortflüssigkeitstest). As for receptive language functions, the subtest “token test” from the Aachener Aphasia Test (AAT) is used widely (35% for adults, 33% for children).

Visuospatial function is assessed with 21 different tests, with little overlap. The most popular test is the copy trial of the ROCFT (35%), which is also used as a figural memory test. All other tests are employed by 20% (i.e., Wechsler Block Design, Judgment of Line Orientation) or 15% of centers (i.e., Hooper Visual Organization Test [VOT], Visual Object and Space Perception Battery [VOSP], Benton Facial Recognition). In children, little agreement (20%) was found regarding the use of the Developmental Test of Visual-Motor Integration (Beery VMI).

As for *motor function*, 18 different tests are in use. Agreement was low for adults and nonexistent for children. For adults, the most popular tests are Finger Tapping (25%), Luria Sequences (25%), and the Purdue Pegboard (15%). For children, no consensus in at least three centers was found.

The monitoring of *emotional and behavioral changes* in patients with epilepsy, is a critical part of their assessment and care given the high incidence of depression, anxiety, aggressive behavior, and organic brain syndrome resulting from the epilepsy itself or its treatment. In adults, the Beck Depression Inventory (BDI or BDI-II) is used in 60% of the clinics, followed by the Hospital Anxiety and Depression Scale (HADS) (25%), the Symptom Checklist 90-R (SCL 90-R, 20%), the Minnesota Multiphasic Personality Inventory (MMPI, 20%), and the Beck Anxiety Inventory (BAI [15%]). For children, most frequently named was the Child Behavior Checklist (CBCL), used by 20% of the centers.

The ultimate goal of treating epilepsy is improving the individual's quality of life. For adults, in 45% of the centers, different versions of the Quality of Life in Epilepsy Inventory (QOLIE) is used (QOLIE-10, QOLIE-31, QOLIE-89). Three centers reported using the Short Form 36 (SF 36) and three clinics reported using a different inventory. No particular quality of life questionnaire was used consistently in pediatric assessment.

The normative data for the tests and questionnaires used in the centers are mostly a variation of published national (92%), international (79%), or local data (33%). Some centers use unpublished local normative data (16%). In general, only 52% of the centers (n = 13) provided us with sources for these normative data (for both children and adults). Sources regarding validity (proof that the test measures what it intends to measure) were provided by 40% (n = 10) of the respondents. However, these sources were not always specific for use in patients with epilepsy. Only five centers (20%) provided sources with evidence supporting the use of the tools in patients with epilepsy. Another five stated that all tests were evidence based, but without citing any sources. We evaluated each of the sources given regarding test validity in detail, considering only sources for tests used

by at least three centers. For adults, 38 sources regarding test validity were reported. These stem from the manual in 36.8% of the references reported, from non-epilepsy-specific publications in 55.3%, and from publications related to epilepsy by 7.9%. With the exception of one WAIS reference, the latter references were related to the QOLIE inventory. With respect to children and adolescents, 12 sources were given regarding the validity of the tests in general or for use in epilepsy. Of these sources, 58.3% were test manuals, 8.3% were publications unrelated to epilepsy, and 33.3% were epilepsy-related publications.

In response to the question which areas of assessment would require further improvement, several were indicated. These included more national normative data, a better test for the assessment of nonverbal memory in relation to right temporal lobe epilepsy, time-efficient tests because of limited personal resources, RAVLT and DCS co-normalization norms for comparison of lateralized temporal lobe functions, and updated QOL questionnaires. Another survey question pertained to functions or behaviors seen in the patients that may elude assessment and for which appropriate tests would be desired. Suggestions were made for evaluating accelerated long-term forgetting, frontal lobe dysfunction, divided visual field, every day performance and external validity of objective performance, mood and behavioral aspects (panic disorder, reaction to stress, organic brain syndrome, and social cognition), and a qualitative scoring of test performance (type of mistakes, performance pattern). Although some tests would allow a more detailed analysis, they are not yet part of a standard diagnostic routine and there is a need for further validation and standardization of these measures.

Assessment of hemispheric dominance

Assessing the dominant hemisphere for language functions is mostly performed by fMRI (in 91%) and IAT (59%), combined with lateralizing tests (91%) such as verbal versus nonverbal memory and inventories (handedness) (Table 5). In single centers, transcranial magnetic stimulation (TMS), magnetoencephalography (MEG), and diffusion tensor imaging (DTI) (arcuate tract) are performed for some cases. Functional transcranial Doppler sonography (fTCD) is used by two centers on a regular basis, with

approximately $n = 33$ and $n = 51$ patients per year, one center using the “Bishop Picture Animation Paradigm” and the other using a word generation and picture description task.

The IAT, although long regarded as the gold standard for evaluation of hemispheric dominance, has increasingly been replaced by noninvasive methods.³¹ The indications differ among the centers (Table 6), from performing the IAT in all cases of TLE of the dominant hemisphere to cases only with the epileptogenic focus in or adjacent to the language cortex ($n = 5$). As for the general approach, bilateral injection in the ACI is still the standard procedure. Anesthetics differ among the centers as well, with amobarbital used most frequently (69%), but in some cases, propofol or methohexital are also used.

Of 20 participants with valid answers concerning fMRI, 20% always perform fMRI in presurgical patients, 55% perform fMRI if the resection is planned in or adjacent to eloquent language areal, 50% if atypical dominance is suspected, 30% if the to-be-resected lesion is located in the (presumably) dominant hemisphere, and 5% perform fMRI in bitemporal cases (multiple answers were possible). Most centers use two (42%) or three (37%) language paradigms, whereas a minority uses only one paradigm (21%). Paradigms are mostly word generation (79%), followed by naming (42%), semantic comparisons (37%), listening (32%), and reading (26%) tasks. Hemispheric dominance is assessed purely visually (50%, $n = 7$) or additionally with a lateralization index (50%). Of the centers that use fMRI on a regular basis, SPM is most often used for analysis (54%, seven centers); other programs were used by one (FSL, BrainVoyager, BrainWave, Neuro3D) or two centers each (NordicBrainEx). Only 2 of 25 centers provided the requested decision tree in this regard.

DISCUSSION

Through our survey, we collected information about the practice of neuropsychological assessment in 25 epilepsy centers across Europe. Our findings demonstrated that neuropsychological assessment is generally perceived as an essential part of the presurgical and postsurgical workup in children, adolescents, and adults.

Table 3. Use of standardized tools for pediatric patients given in percentages

	Developmental scales		Standardized tests		Intelligence tests		Personality and mood	
	N	%	N	%	N	%	N	%
Babies (infants)	10	83.33	9	75	2	16.67	1	8.33
Toddlers	9	69.23	10	76.92	6	46.15	3	23.08
Preschool children	11	68.75	16	100	12	75	7	43.75
School children	10	58.82	17	100	17	100	11	64.71
Adolescents	9	50	18	100	18	100	13	72.22

Table 4. Tests used in the different centers for (a) children and adolescents; (b) adults

Test	Used by (%)	Validity	Normalization
(a)			
Intelligence			
Wechsler Intelligence Scale for Children (WISC, WISC-III, WISC-IV, WISC-R)	60	1	1, 1, 1
Wechsler Preschool and Primary Scale of Intelligence (WPPSI, WPPSI-III, WPPSI-IV)	33	0	0
Other (n = 10)			
Developmental scales			
Bayley Scales of Infant Development	33	2, 3	1
Vineland Adaptive Behaviour Scale (VABS)	20	0	0
Denver Developmental Screening Test	20	0	1
Other (n = 4)			
Nonverbal memory			
Diagnosticum für Cerebralschädigungen (DCS and DCS-R)	20	1	1, 1, 1, 3
Other (n = 7)			
Verbal memory			
Verbaler Lern- und Merkfähigkeitstest (German RAVLT equivalent)	20	3, 3	1
Other (n = 8)			
Attention and executive functions			
Digits (Wechsler Memory Scale subtest)	40	1, 1	1, 1
A Developmental Neuropsychological Assessment (NEPSY/II)	33	1	1
Trail Making Test (TMT) A and B	27	2	0
Corsi (Wechsler Memory Scale subtest)	27	1, 1	1, 1
Other (n = 18)			
Language			
Token test	33	0	1, 1
Boston Naming Test	33	0	0
Other (n = 20)			
Visuospatial functions			
Developmental Test of Visual-Motor Integration (Beery VMI)	20	0	0
Other (n = 15)			
Motor functions			
No consensus of >3 centers n = 17			
Mood and behavior			
Child Behavior Checklist (CBCL)	20	0	1
Other = 12			
Quality of life			
No consensus of >3 centers n = 7			
(b)			
Intelligence			
Wechsler Adult Intelligence Scale (WAIS)	90	0	3
WAIS-III	40		
WAIS-IV	30		
WAIS	15		
WAIS-R	5		
WASI and other abbreviated versions	15	0	0
Raven progressive matrices	15	0	0
Mehrfach-Wortschatz-Intelligence (MWT-B)	15	1	1
Other (n = 3)			
Nonverbal memory			
Rey-Osterrieth Complex Figure Test (ROCFT)	55	0	0
Diagnosticum für Cerebralschädigungen (DCS and DCS-R)	20	1	0
Benton	15	0	1
Other (n = 7)			
Verbal memory			
Rey Auditory Verbal Learning Test (RAVLT)	40	1	0
Logical memory (Wechsler memory scale subtest)	25	0	0

Continued

Table 4. Continued.

Test	Used by (%)	Validity	Normalization
Other (n = 10)			
Memory batteries			
Wechsler Memory Scale (WMS)	20	1, 2	0
Recognition Memory Test (RMT)	15	0	0
Other (n = 3)			
Attention and executive			
Corsi and digits (Wechsler Memory Scale subtest)	70	1, 1, 2	1, 1
Trail Making Test (TMT) A and B	60	2, 2, 2, 2	2, 2
Stroop test	45	2, 2, 2	2, 1
D2	30	0	0
TAP (Testbatterie zur Aufmerksamkeitsprüfung)	15	0	1
WCST (Wisconsin Card Sorting Test)	15	2	1
Other (n = 29)			
Language			
Boston Naming Test	75	1, 2	1, 2
Phonemic fluency	45	2, 2, 2,	2, 2, 2, 2, 2
Semantic fluency	40	2	2
Token test	35	0	2
Other (n = 23)			
Visuospatial			
Rey-Osterrieth Complex Figure Test, Copy (ROCFT)	35	1	1
Block design (Wechsler Intelligence Scale subtest)	20	1, 2	1, 2
Judgement of line orientation test	20	0	0
Hooper Visual Organization Test (VOT)	15	2	2
VOSP (Visual Object an Space Perception Battery)	15	1	1
Benton facial recognition	15	0	1, 2
Other (n = 14)			
Motor functions			
Tapping	25	1	0
Lurja sequences	25	1	1
Purdue Pegboard	15	0	0
Other (n = 15)			
Mood and behavior			
Beck's Depression Inventory/BDI-II	50	1	1, 2
HADS	25	1	1
SCL 90 R	20	2, 2	2, 2
MMPI	20	2	1, 2
BAI	15	0	0
Other (n = 20)			
Quality of life			
Quality of Life in Epilepsy Inventory (QOLIE)	45		
QOLIE ^a	15	3	3
QOLIE 31	15	3	3
QOLIE 10	10	0	0
QOLIE 89	5	3	0
Short Form 36	15	2	2
Other (n = 3)			

Listed are tests that are used by at least three of the centers. Percentages refer to the number of valid answers of clinics providing neuropsychological assessment in children (n = 15) and adults (n = 20). References were requested for normative data in healthy controls and/or patient groups, and for the validity of the test. Cited references were classified into no evidence given (0), test manual (1), published evidence that is nonspecific for epilepsy (2), and published evidence specific for the use in epilepsy patients (3). Each of these numbers represents one cited source.

^aNonspecified QOLIE.

In most E-PILEPSY-associated centers, neurosurgery and neuropsychology are performed in-house or close by, so that the conditions are optimal for short communication pathways and multidisciplinary patient care.

According to the survey, the primary indications for neuropsychological evaluation are the assessment of the overall level of cognitive functioning; assessment of particular

functions, as well as ictal and postictal testing for localization diagnostics (discerning the relationships between structure and seizure focus to cognitive function); determination of language dominance, negative cognitive antiepileptic drug effects, postsurgical follow-up, and outcome control; and the need for rehabilitative care. In children, evaluation and monitoring of neurodevelopment is also a major

Table 5. Methods for assessing hemispheric dominance for language functions

Method	Percentage	N
Lateralizing (memory) tests	91	20
fMRI	91	20
Hand dominance	86	19
IAT	59	13
Dichotic listening	32	7
TMS	14	3
fTCD	9	2
MEG	5	1
DTI	5	1

fMRI, functional magnetic resonance tomography; IAT, intracarotid amobarbital test; TMS, transcranial magnetic stimulation; fTCD, functional transcranial Doppler sonography; MEG, magnetoencephalography; DTI, diffusion tensor imaging.

Methods for assessing hemispheric dominance for language functions. Valid answers given by n = 22.

indication. As for the structural and methodological aspects of neuropsychological assessment in epilepsy, the European centers are largely in line with recent recommendations by the ILAE neuropsychology task force.²⁰

In times of limited personnel capacity (neuropsychological staff consists on average of 2.5 psychologists, with an average number of 171 patients tested per year and an average time of 4.5 h for a presurgical evaluation (see Table 2); it seems impossible to perform a thorough

neuropsychological assessment with every patient receiving all tests and procedures. Instead, a core test battery should be compiled that can be extended optionally, depending on specific questions in terms of a modular diagnostics.

In terms of the cognitive domains that the centers rated as most essential, there was a high consensus (64–90%) regarding the necessity to assess memory, language, attention, and executive functions. The order of the listing corresponds to the fact that most surgical candidates have temporal lobe epilepsy (affecting memory and language) followed by frontal and posterior epilepsies (affecting attention, executive functions, language, visuoconstruction, and motor functions). Tests for primary and secondary posterior perceptual (i.e., visual, auditory, and tactile functions) were largely not considered and are probably less relevant. Of interest, IQ testing was considered as necessary by less than one third of the centers working with children and adults (5/18, 27.8%), but for 75% (3/4) of centers testing only children. In young children, developmental scales are widely used, and assess the domains of psychomotor, cognitive, and language development. The assessment of particular functions in children was reported as well, but as demonstrated in the literature, localization and lateralization diagnostics are difficult when examining the young brain, which is still in the process of developing and specializing.

Table 6. Protocols and methods for performing functional magnetic resonance imaging and the intracarotid amobarbital test for assessing the hemispheric dominance for language functions

	fMRI (n = 20)	%	N	IAT (n = 13)	%	N
Patients per year	M = 37.97 (SD = 54.36) Range: 2–250			M = 6.55 (SD = 4.33) Range: 2–15		
Indication (multiple responses)	Epilepsy in eloquent area	55	11	Noninvasive methods inconclusive	62	8
	Atypical dominance suspected	50	10	fMRI not possible	46	6
	Epilepsy in dominant hemisphere	30	6	Lesion in eloquent area	38	5
	All presurgical patients	20	4	Risk of global amnesia	15	2
Protocol	Word generation	79	15	Lesion in dominant hemisphere	8	1
	Naming	42	8	Naming	92	12
	Semantic comparison	37	7	Verbal memory	77	10
	Listening	32	6	Figural memory	77	10
	Reading	26	5	Counting	69	9
	1 paradigm	21	4	Reading	62	8
	2 paradigms	42	8	Body commands	54	7
	3 paradigms	37	7	Picture pointing	54	7
				Comprehension	54	7
				Repetition	46	6
Approach	Laterality index	50	7	Spontaneous speech	38	5
	Visual analysis	50	7	Bilateral (vs. unilateral)	77	10
	SPM	53.9	7	Only nonselective (ACI)	85	11
	NNLBrainEX	15.4	2	Selective in single cases	15	2
	FSL	7.7	1			
	Neuro3D	7.7	1	Amobarbital	69	9
	Brain Voyager	7.7	1	Methohexital	15	2
	BrainWave	7.7	1	Propofol	15	2

The total number of tests and questionnaires reported in the present survey as being in use for patients with epilepsy was vast ($n = 186$). Based on frequency statistics, good candidates for a core battery on which centers might agree could be found for most domains (see Results section, Which test instruments are currently used? Neuropsychological tests and questionnaires). This selection is not meant to be a recommendation, but rather a reflection of the current practice. This list is highly dependent on the availability of the individual tests in the specific countries or languages, and does not necessarily reflect the degree of evidence for the use of the tools in patients with epilepsy. For some countries, some consensus might already exist on a national level. In Germany, a working group with all neuropsychologists in epilepsy centers, as well as a working group for presurgical diagnostics and epilepsy surgery associated with the national ILAE chapter, has been established. Its members meet at regular intervals and are dedicated to harmonizing and improving assessments in Germany.^{26,27,32}

Neuropsychological assessment should not be an end in itself. It should provide information about the patients that is useful for clinical decision making. Indeed, according to the responses in the present survey, neuropsychological testing played an important role in decision-making by influencing therapeutic decisions and counseling of patients in regard to possible cognitive sequelae of surgery, as well as determining the extent and timing of the surgery. Apart from the presurgical workup per se, neuropsychology also helps to optimize treatment with AEDs, indicates the necessity to assess language dominance in cases of atypical memory profiles, leads to referrals to rehabilitation programs when detecting significant post-surgical impairments, and indicates the necessity for psychiatric care and treatment in cases of severe depression, psychosis, or mental decline/dementia, or the initiation and/or termination of immune-modulatory therapies (in cases of autoimmune encephalitis). Apart from exhaustive assessment, postictal testing of basic cognitive functions is an important aspect of the presurgical diagnostic procedure, as it may indicate the hemisphere or site of epileptogenic seizure focus. This includes testing of language functions for lateralization of seizure origin.

Given the aforementioned consequences of neuropsychological evaluations for patients and treatment decisions, it is well understood that the tests in use should be valid and reliable for people with epilepsy. Purely performance-oriented testing does not necessarily meet the requirements of a sophisticated presurgical evaluation in epilepsy patients and might even be irresponsible if such nonspecific knowledge is used for counseling, or when expected or predictable deficits cannot be detected or predicted. As evident in a well-known example, had only IQ testing been performed in the amnesic patient H.M., the catastrophic outcome of bilateral amygdalohippocampectomy would have been overlooked.³³

For this reason, all centers were asked to cite the sources that would demonstrate the validity of the tests in use with regard to detecting the effects of epileptogenic lesions, seizures/epileptic activity, epilepsy surgery, and pharmacologic treatment. Here, many sources were cited concerning the normalization and general validity of the tools used, that is, that a memory test is indeed measuring memory and that it has age-based norms and so on, but surprisingly few references were given addressing the validity of these tests in epilepsy. This may mean that the test selection is not based on evidence for their use in epilepsy, that there is no evidence, or that this question was skipped because of a lack of time, or simply because there was a limited number of adequate tests available in certain centers.

Whatever the reason for the present results, our findings parallel those of a national survey²⁴ that showed that only one third of the tests were evidence based for use in epilepsy, another third were reported to have been normalized and standardized independent of epilepsy, and one third were chosen based on personal preferences.

The second part of this present study addressed hemispheric dominance assessment. It showed a high agreement on the methods in use. Almost all centers use fMRI in addition to lateralizing cognitive tests and handedness inventories. Many centers still use the IAT,³⁴ but only in single select cases and not as part of standard care. Generally, there appears to be some uncertainty regarding the individual use and application of measures for the determination of lateral dominance tests. This is indicated by the lack of agreement on the circumstances that would indicate the necessity of IAT and fMRI, reflecting the type of information these methods can contribute. Similar to the pattern of responses regarding neuropsychological assessment, heterogeneity was found in regard to the fMRI paradigms in use. Given the frequent use of fMRI for preoperative lateralization and localization of cognitive function, however, the development of standardized fMRI protocols to assist in clinical decision-making on an individual level seems worthwhile. The rare use of the IAT reflects the steady decline of indications for the IAT, as reported in the literature. The remaining few cases in which it is used highlights the type of information it can provide and predict.

CONCLUSION

The general principles of neuropsychological testing were evaluated across European epilepsy centers and are consistent with what has recently been formulated by the neuropsychology task force of the ILAE.²⁰ This is encouraging, as this knowledge provides a foundation that will inform future recommendations regarding which tests (minimum standards) should be used in the presurgical and post-surgical care of persons with epilepsy. Similar to Marilyn Jones-Gotman's milestone work 23 years ago,²¹ however, there is still significant heterogeneity among centers with

regard to the tests that are used. Nevertheless, a subset of tests can be highlighted for the most essential cognitive and behavioral domains that appear to be good candidates for a core battery across the E-PILEPSY-associated centers. Because only a minority of the tests in use were or could be justified on the basis of published evidence for their use in epilepsy, the essence of the survey shows that the final selection of tests will need to be based on the best evidence (ongoing systematic review), the current survey, and, for many, expert consensus methodology (until further evidence is available). Finally, as regards the assessment of hemispheric dominance, the lack of common paradigms raises the question of when these results are really essential for clinical decision-making. Here additional work is required involving the comparison of methods and paradigms in order to elucidate the precise decision making procedure for the individual patient.

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