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The practice of Deep Brain Stimulation

**An update based on an international
survey about clinical and ethical issues**

Markus Christen,

University of Zurich & University of Notre Dame

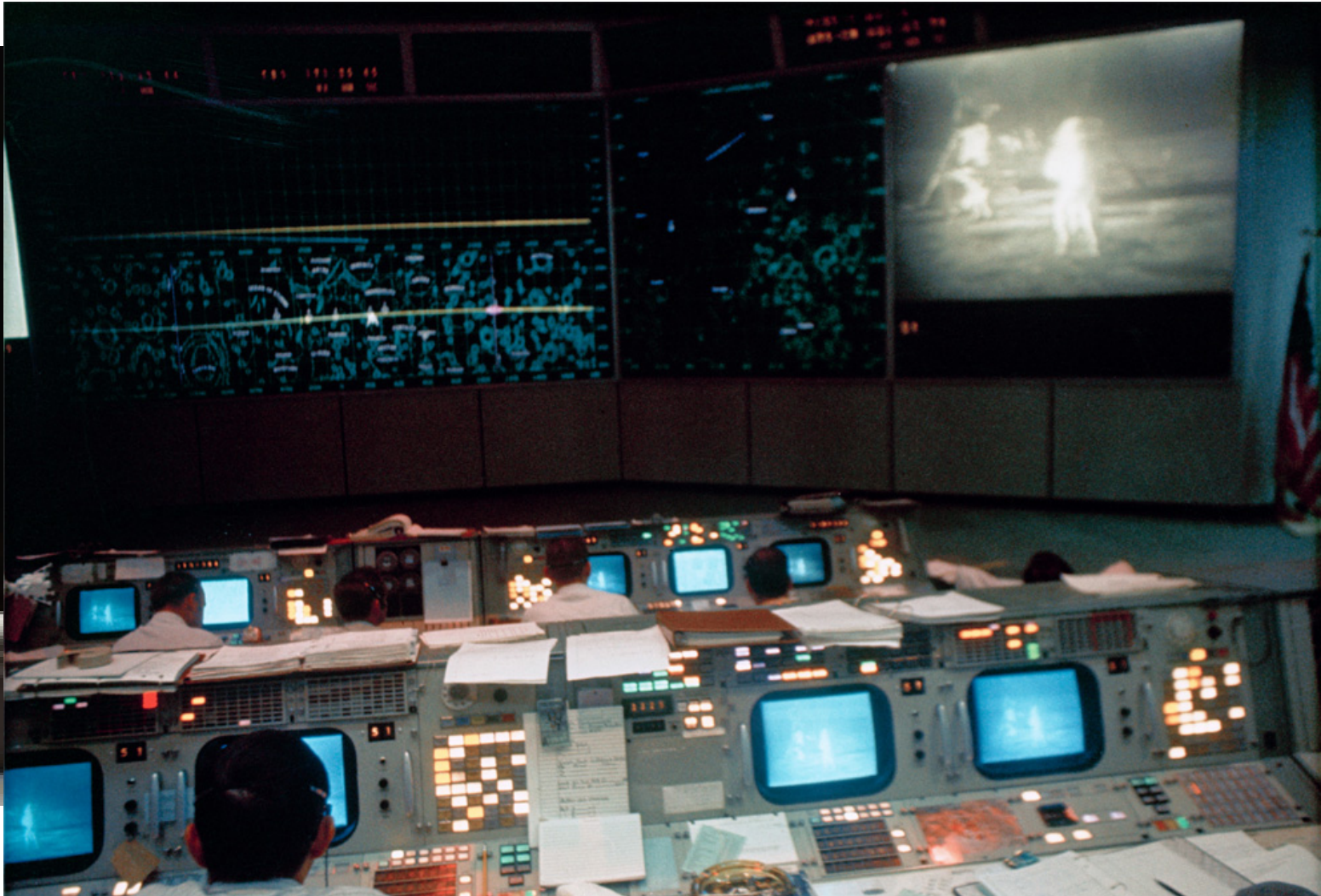




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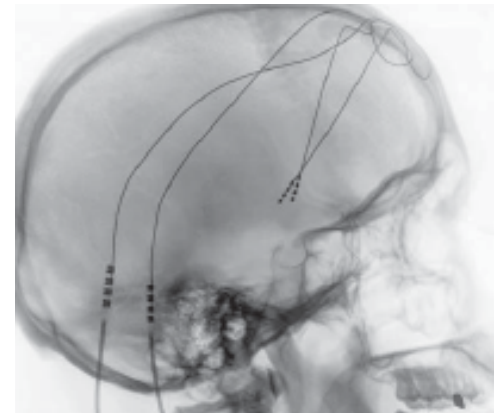
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Deep Brain Stimulation - A short overview



What is DBS?

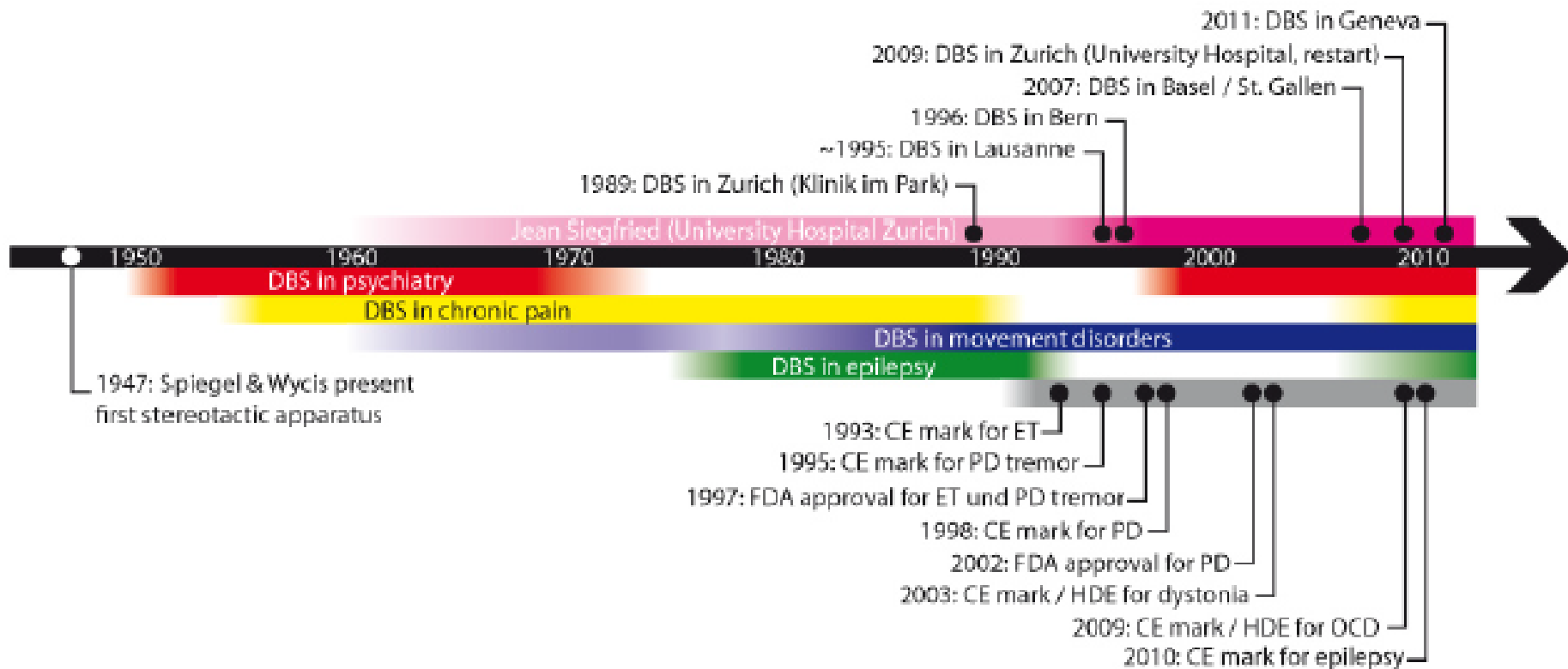
- **Deep brain stimulation:** applying a continuous, high-frequency current via electrodes in specified subcortical regions of the brain.
- Emerged out of **pacemaker-technology** (up to recently only one major supplier: Medtronic).
- **Target localization** based on ablative surgery (“lesions”) and increasingly also on theories how neuronal networks realize brain functions.
- **Chirurgical intervention** is relatively safe. Periodic local surgery for battery change (frequency depends on stimulation parameters)
- **Stimulus parameters:** monopolar cathodic square pulses (1-5 V amplitude, 120-180 Hz frequency), have to be adjusted after surgery, patient may control stimulator to some extend.
- Mostly a “**last resort**” option (but that is changing for movement disorders).



Parkinson Schwelz, 2012



Historical overview

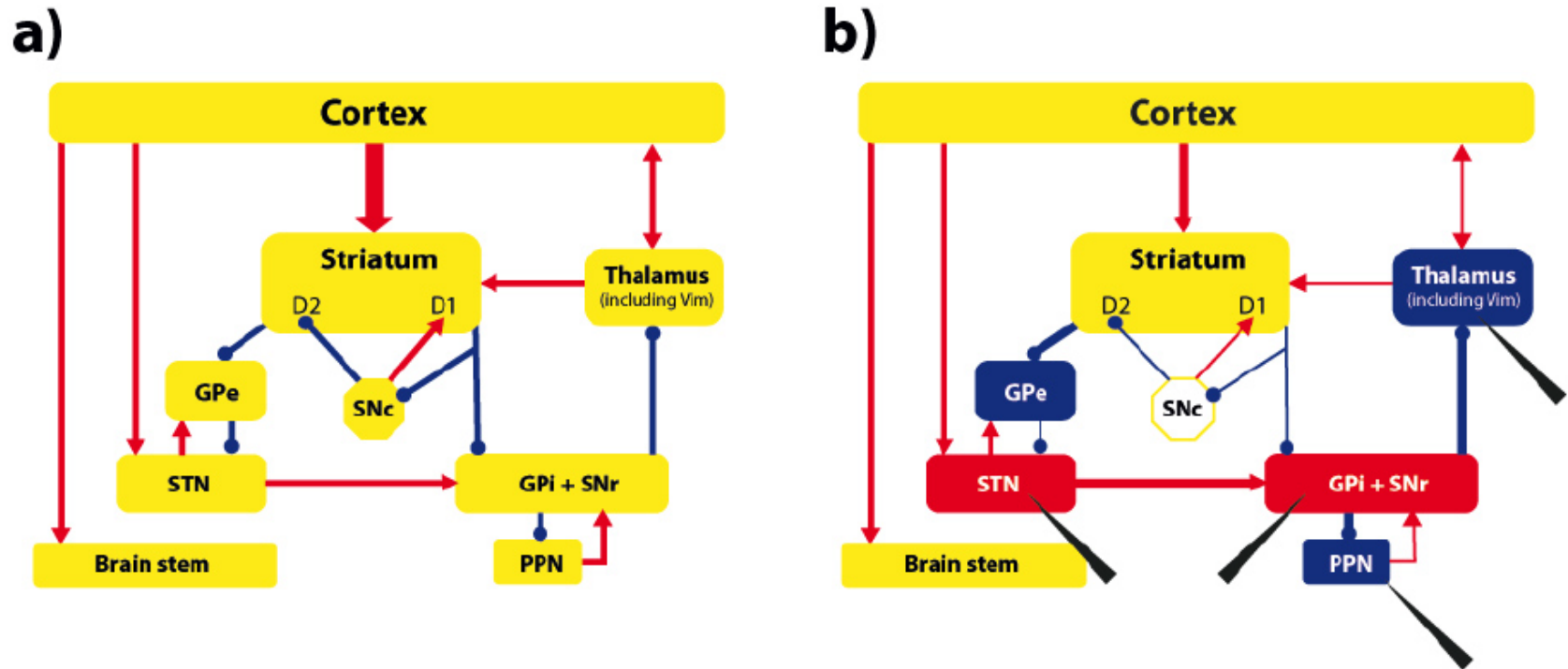


Christen & Müller, 2012



DBS in movement disorders

An illustration of a much more technological (circuit) – driven way to frame the problem compared to medication-based approaches:



Christen & Müller, 2012



DBS in numbers

Number of patients (estimations partly based on unit sales, i.e. over-estimation), i.e. global “DBS-population” late 2006: 35,000

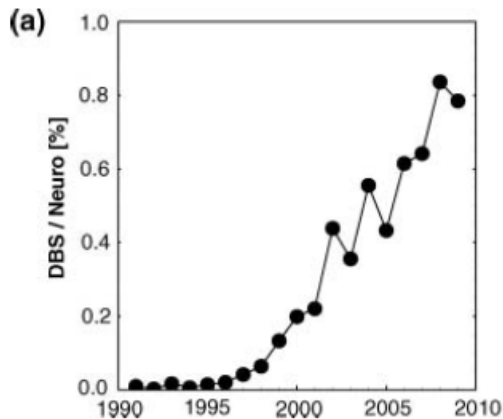
January 2010: 75,000

January 2011: 85,000

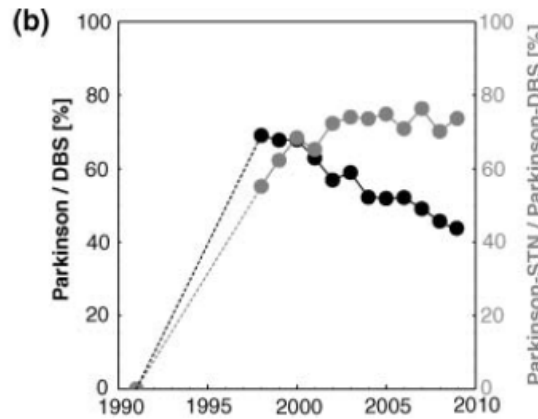
Estimation of annual number of surgeries (only USA): 2,500 – 4,000

Globally (lower and upper bounds, own research): 5,000 – 10,000

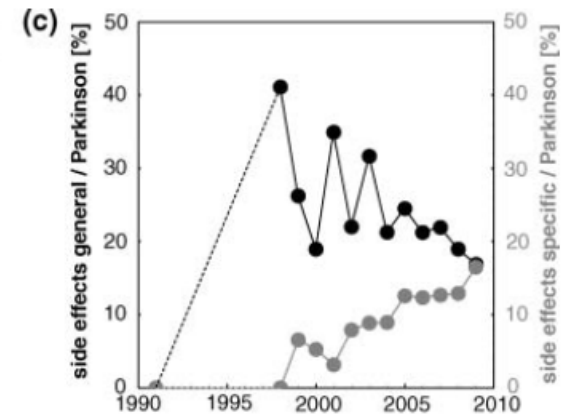
Bibliometry (# publications):



1/30/2013



Müller & Christen, 2011



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Approaching the “System DBS”: two dimensions



A broad spectrum of therapeutic and side effect

Group 1: Main therapeutic issues

Group 2: Intervention related issues

Group 3: Issues concerning behavior, cognition, mood, sociality.

Group 4: Other issues

Table 2. Issue classes of therapeutic effects and side effects present in the STN-DBS literature

Group	Abbr.	Issue class	Examples of side effects
Group 1	F	Functional studies, i.e., studies that involve PET or other methods for investigating the causal effect of DBS	—
	M	Motor effects	Apraxia, axial symptoms, dyskinesia, dystonia, gait disorders, motor fluctuations
	V	Issues related to Levodopa and other medication	Dopamine dysregulation syndrome, changes in LEDD
Group 2	O	Operation/surgery related issues	Hemorrhage, hematoma, ischemia, surgical complications, infections
	P	Patient issues, i.e., issues related to patient selection, patient management, rehabilitation	—
	T	Effects related to the technology (device)	Battery problems, electrode break, local infections, lead fracture, pulse generator malfunction
Group 3	B	Behavioral effects, i.e., effects that concern abnormal behavior	Compulsive shopping, hypersexuality, hypomania, pathological gambling, suicide (attempts)
	C	Effects on cognition (reasoning, memory, etc.)	Cognitive decline, confusion, dementia, memory decline, verbal fluency change
	D	Depression, anxiety, apathy and other mood effects	Ahedonia, apathy, depression, mood changes, sadness
	L	Language, i.e., effects regarding the general speech ability and motor aspects of speech	Aphasia, dysarthria, hypophonia, speech impairment, voice freezing
	Q	Quality of life and social aspects	Disability in daily living, decreased life satisfaction, partnership problems
Group 4	A	Effects regarding the autonomous nervous system, autonomous functioning	Drooling, dysphagia, hyperhidrosis
	E	Emotion recognition changes	Difficulties of emotion discrimination, difficulties of face perception, hyperemotivity
	I	Insomnia, i.e., effects related to sleep	Drowsiness, fatigue, insomnia, sleep disorders
	K	Cost issues (German: <i>Kosten</i>), i.e., cost-benefit studies, cost-effectiveness of DBS, etc.	—
	N	Other neurological effects	Epilepsy, postural imbalance, seizures
	S	Effects regarding sensory systems	Blurred vision, parasthesia, visual hallucinations
	W	Weight and energy intake changes	Abnormal weight gain, binge eating, obesity



Broadening of the spectrum (1: publications)

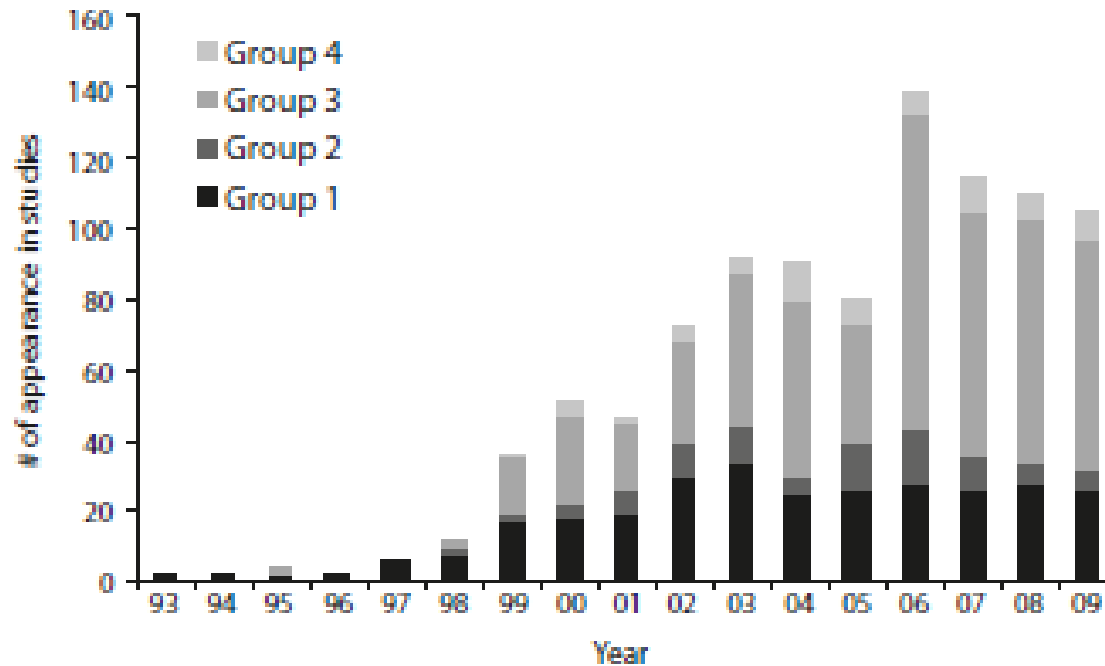
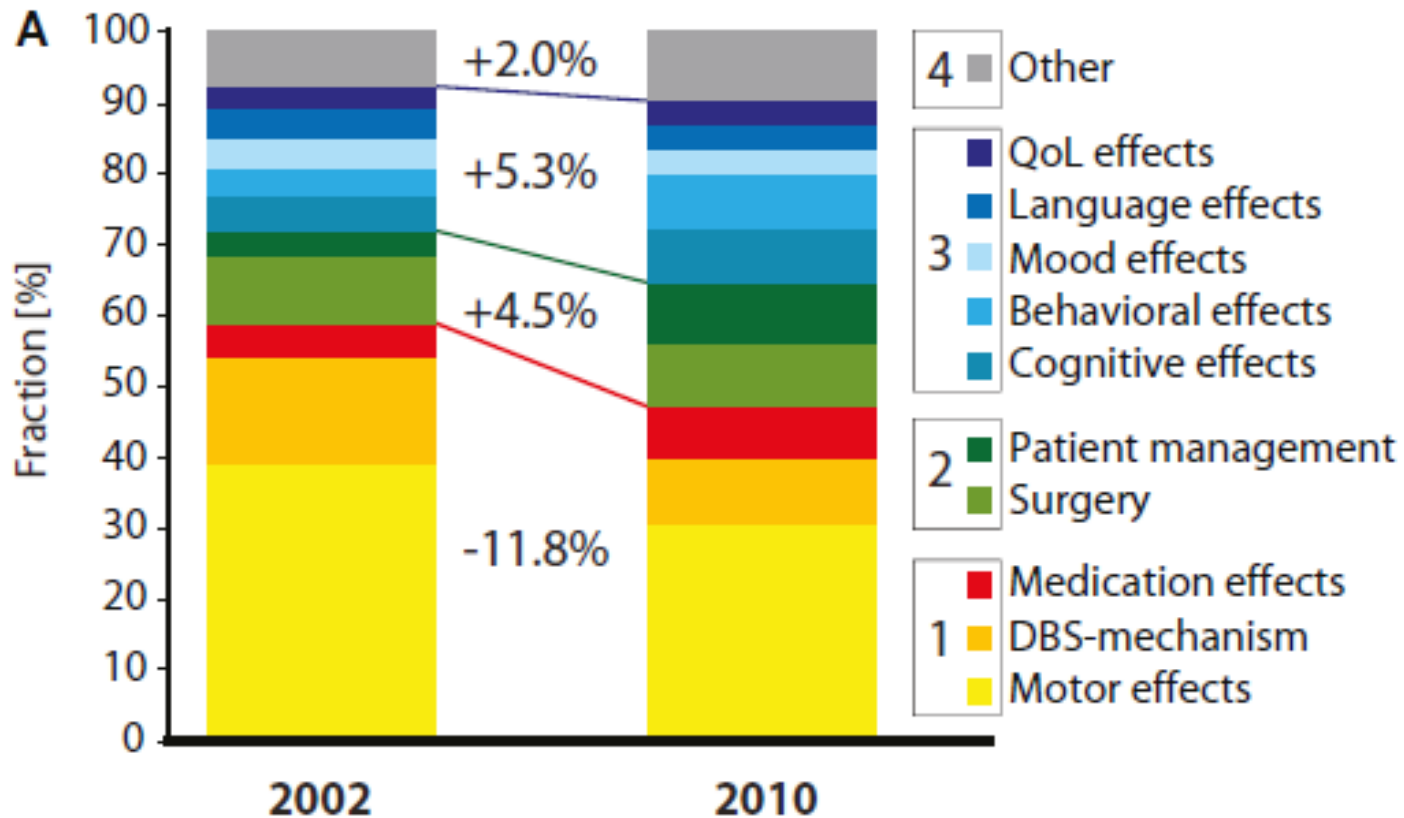


Figure 1. The histogram displays the total number of issues (compare with Table 2) addressed in the publications about STN-DBS (case reports, reviews, and outcome studies) pooled in four groups (group 1: F, M, V; group 2: O, P, T; group 3: B, C, D, L, Q; group 4: A, E, I, K, N, S, W; see text).



Broadening of the spectrum (2: posters)



Christen & Müller, 2011



Some shortcomings identified in the DBS community

Quality of research (11 criteria)

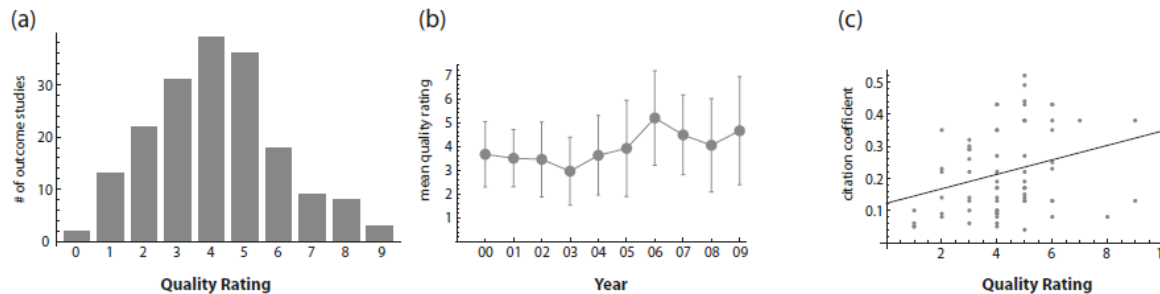
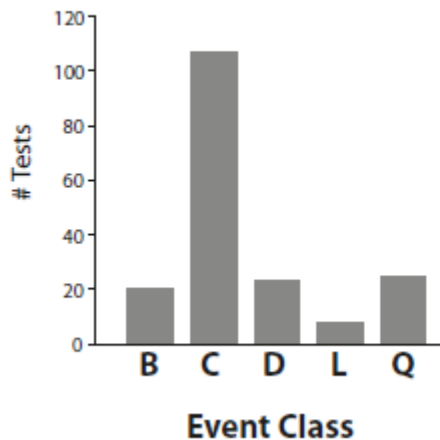
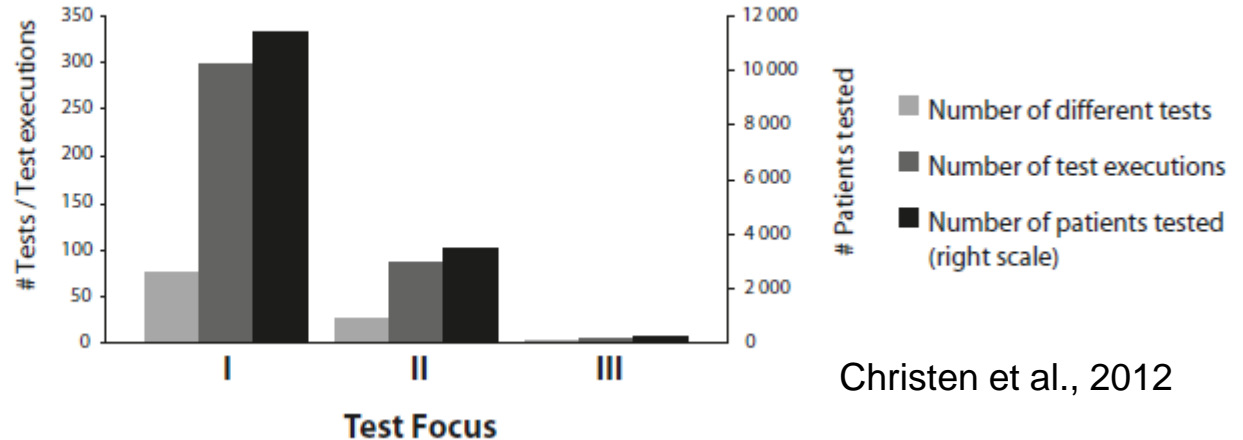


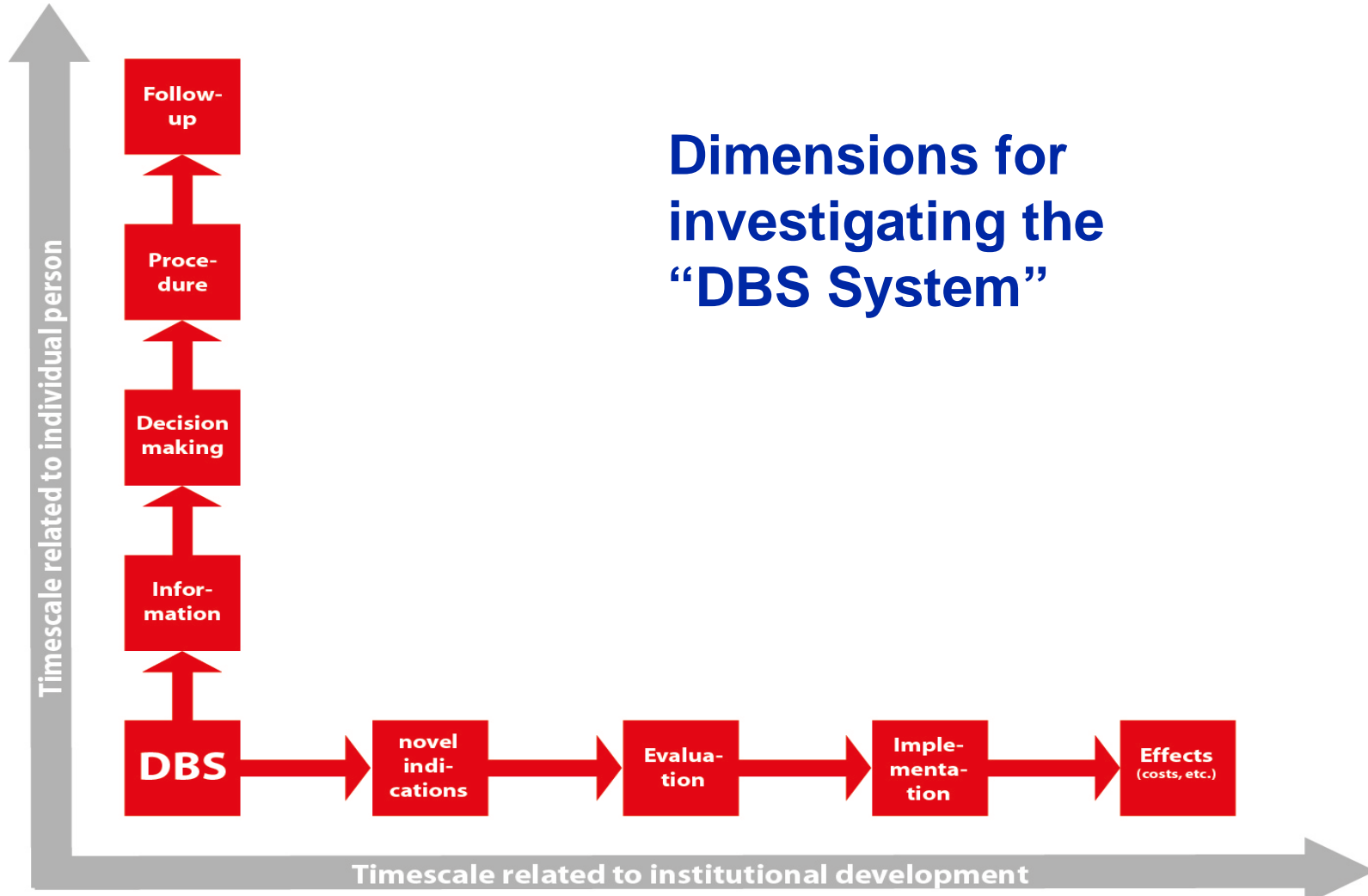
Figure 2. (a) Quality rating distribution of the outcome studies of group 3, (b) time course of the mean quality rating of outcome studies (group 3), and (c) correlation between the citation coefficient of studies (which reflects the appreciation of papers by the authors of reviews) with the quality rating of the studies. The chart also includes the linear approximation of the correlation.

(a) Focus of outcome



(b)







Two surveys: Experts and Centers

Researchers / clinicians: 679 persons identified, 113 (16.6%) answered. *Several indications show that we have received answers from experienced researchers and clinicians.*

Centers in 12 countries: 406 centers identified, 132* (32.5%) answered.

Expert survey	
Professions	Neurosurgeons (47%), Neurologists (40%), Neuropsychologists (8%), Psychiatrists (2%), other (3%)
Age-groups	up to 39 (24%), 40 to 49 (27%), 50 to 59 (32%), 60 or more (5%), no answer (12%)
Gender	male (72%), female (18%), no answer (10%)
Place of work	USA (23.9%), Germany (13.3%), France (12.4%), Italy (12.4%), UK (4.4%), Canada (3.5%), Japan (3.5%), Switzerland (3.5%), Sweden (2.7%), Netherlands (1.8%), Spain (0.9%), other (5.3%), no answer (12.4%).
Center survey	
response rate per country	Australia (50.0%), Canada (54.5%), France (44.0%), Germany (31.8%), Italy (53.3%), Japan (23.3*), Netherlands (50.0%), Spain (35.7%), Sweden (33.3%), Switzerland (100.0%), UK (28.6%), and USA (23.6%)



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The “intervention dimension”



Patient information

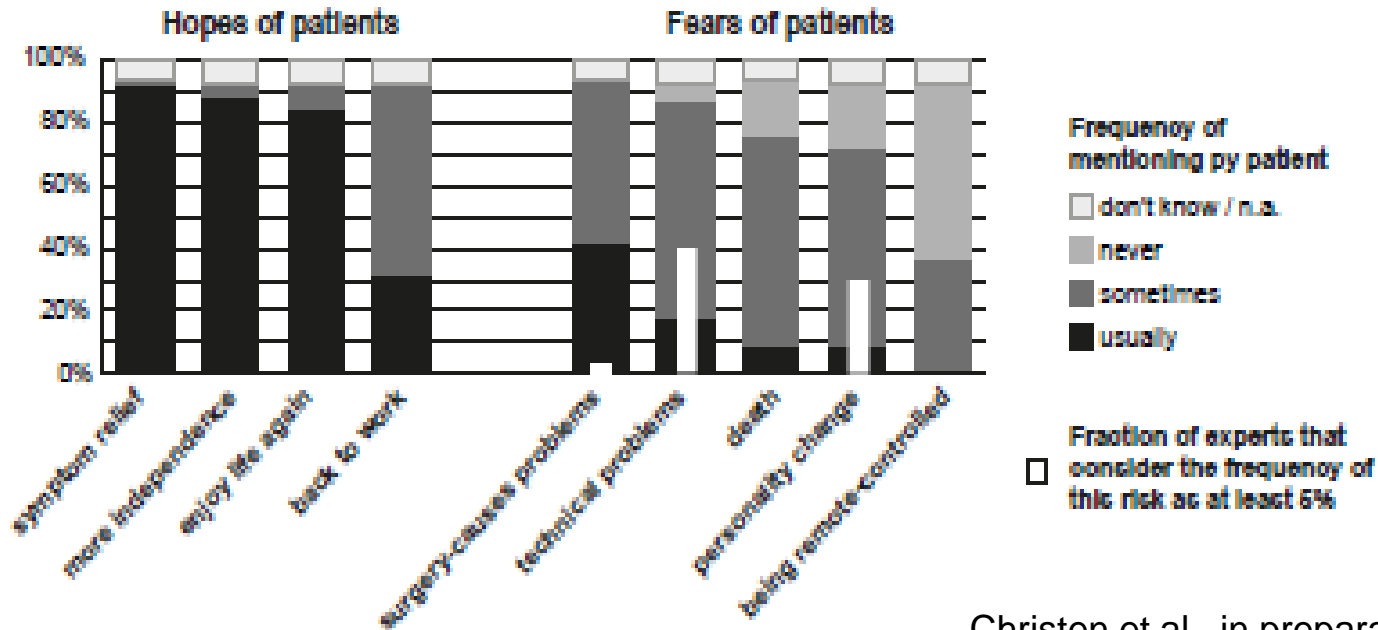
Neurologists (in private practice) are the major entry point into the “DBS system”

Information sources of the patient				
Neurologist in private practice	76.1%	19.5%	0.9%	3.5%
Physician of the DBS institution	53.1%	30.1%	8.8%	8.0%
Internet	53.1%	42.5%	0.0%	4.4%
Support groups	47.8%	40.7%	5.3%	6.2%
Brochure of the DBS institution	42.5%	31.0%	17.7%	8.8%
General Media	31.0%	50.4%	8.0%	10.6%
Family and friends	24.8%	67.3%	1.8%	6.2%
Brochure of the device producer	23.9%	46.9%	21.2%	8.0%
General practitioner	11.5%	53.1%	22.1%	13.3%
Scientific literature	12.4%	58.4%	17.7%	11.5%
Referral of the patient by...				
...neurologist in private practice	91.2%	8.0%	0.0%	0.9%
...other medical institutions	47.8%	41.6%	6.2%	4.4%
...departments of the same Institution	37.2%	38.9%	12.4%	11.5%
... himself/herself (self-referral)	20.4%	48.7%	20.4%	10.6%
... the general practitioner	15.9%	59.3%	19.5%	5.3%
	Usually / often	sometimes	never	n.a. / don't know



Decision Making

There is some mismatch between fears patient mention frequently and the actual risks.



Christen et al., in preparation



Procedure

There are some indications of a “habituation effect”, i.e. less disciplines are routinely involved in DBS surgery than the complexity of the disease/intervention would require.

	routinely involvement of disciplines in intervention				
	core-disciplines	neuro- /psychology	psychiatry	care & rehabilitation	social work
Expert survey	100.0%	85.7%	42.0%	41.1%	21.4%
Center survey	100.0%	68.5%	45.4%	45.4%	16.9%

Christen et al., in preparation



Follow-up (1)

DBS experts tend to underestimate the frequency of some side effects after the intervention.

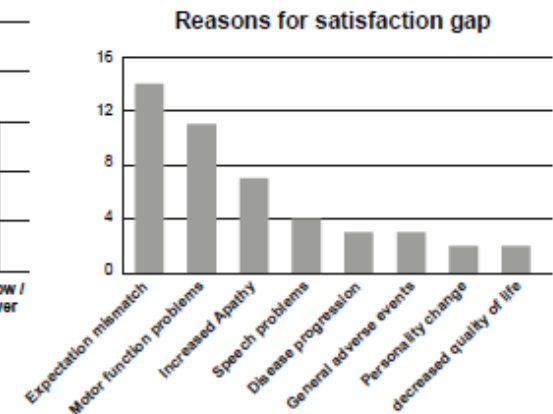
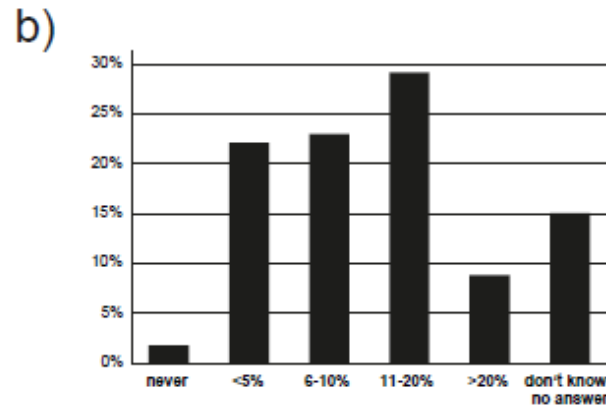
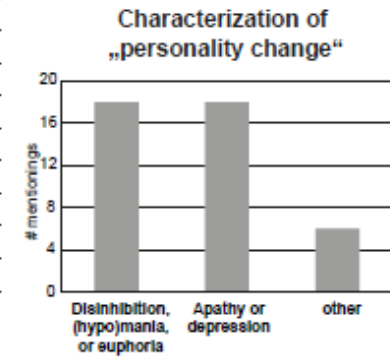
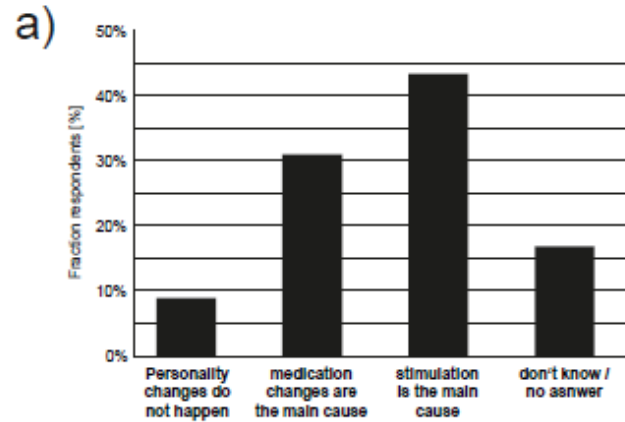
	< 1%	1-5%	6-10%	11-20%	>20%	d.k. / n.a.	Literature
Apathy	27.4%	26.5%	15.9%	15.0%	2.7%	11.5%	12-25%
Language problems	20.4%	33.6%	22.1%	8.0%	5.3%	10.6%	9.3%
Device failures	23.0%	30.1%	29.2%	5.3%	1.8%	10.6%	4-15%
Personality change	23.9%	38.1%	15.0%	7.1%	4.4%	11.5%	<0.5-2%
Depression	16.8%	44.2%	20.4%	4.4%	1.8%	12.4%	5-25%
Anxiety	35.4%	30.1%	10.6%	7.1%	1.8%	15.0%	2-18%
Hemorrhage	67.3%	19.5%	0.0%	1.8%	0.9%	10.6%	0-4%

Christen et al., in preparation



Follow-up (2)

Complex changes in behavior (“personality changes” and the “satisfaction gap” seem to be more common problems than expected.





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The “institution dimension”



Differences in capacities of centers in 12 countries

Even in the top-DBS-research countries the predicted eligibility rate (for PD patients) differ by a factor 5.

The US, Switzerland, Sweden and Germany seem to have the highest capacity allowing for an expansion of the indication spectrum.

	AUS	CAN	CHE	DEU	ENG	ESP	FRA	ITA	JPN	NLD	SWE	USA
# responding centers	5	6	7	14	3*	10	11	16	7*	4	2	45
total capacity of responding centers	237	196	193	562	73	296	336	255	235	140	73	2,655
total # of centers	10	11	7	44	16	28	25	30	30	8	6	191
estimated capacity per year	470	360	200	1770	390	830	760	480	1,000	280	220	11,270
predicted estimated eligibility rate	11.6-26.1%	5.8-13.1%	13.9-31.3%	12.0-27.0%	4.1-9.2%	9.8-22.0%	6.5-14.5%	4.4-9.9%	4.4-9.9%	9.3-21.0%	12.9-28.9%	19.9-44.8%



Indications (1)

The literature reveals a growing expansion of DBS indications that is confirmed by our survey.

Established indications

- Parkinson's' disease
- Essential Tremor
- Dystonia
- (Tourette)
- (OCD)
- (Pain)
- (Epilepsy)

Indications that probably soon will be established

- Major Depression

Indications in research (& proposed)

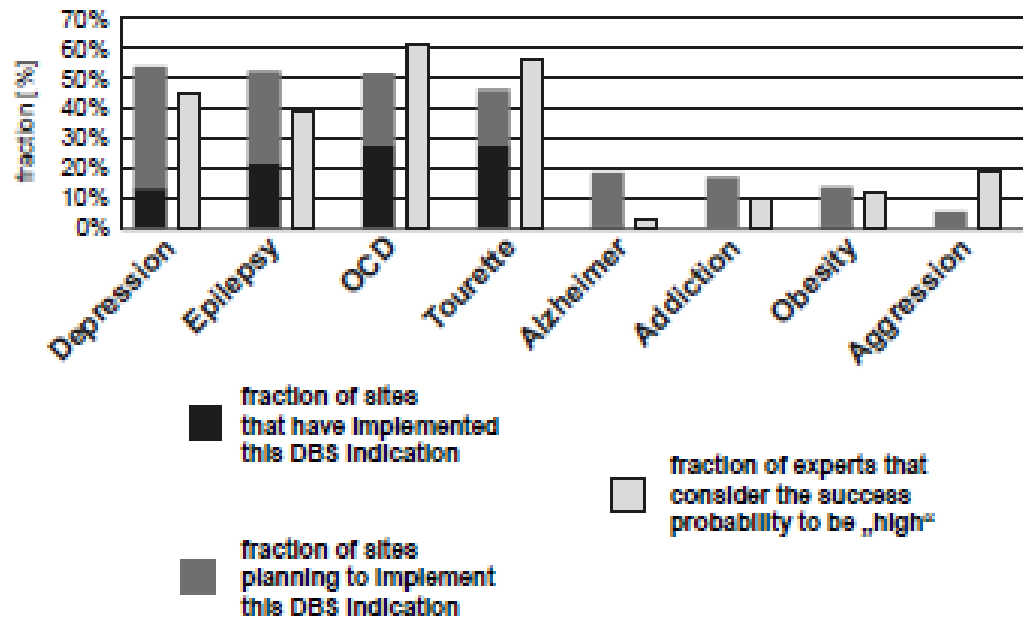
- Addiction (various forms)
- Alzheimer's disease
- Chorea Huntington
- Disorders of consciousness
- Hypertension
- Memory impairment
- Obesity / Anorexia
- Schizophrenia
- Severe auto-aggression
- Other movement disorders (e.g. myoclonus)
- Pain (novel forms)

	PD	ET	DYS	TOU	OCD	MDD
Expert-centers	98.2%	93.8%	92.9%	50.4%	46.0%	32.7%
Center survey	97.7%	94.6%	87.7%	27.7%	27.7%	13.1%



Indications (2)

Not all indications “in research” share high appreciations by the DBS experts (with respect to success probability).

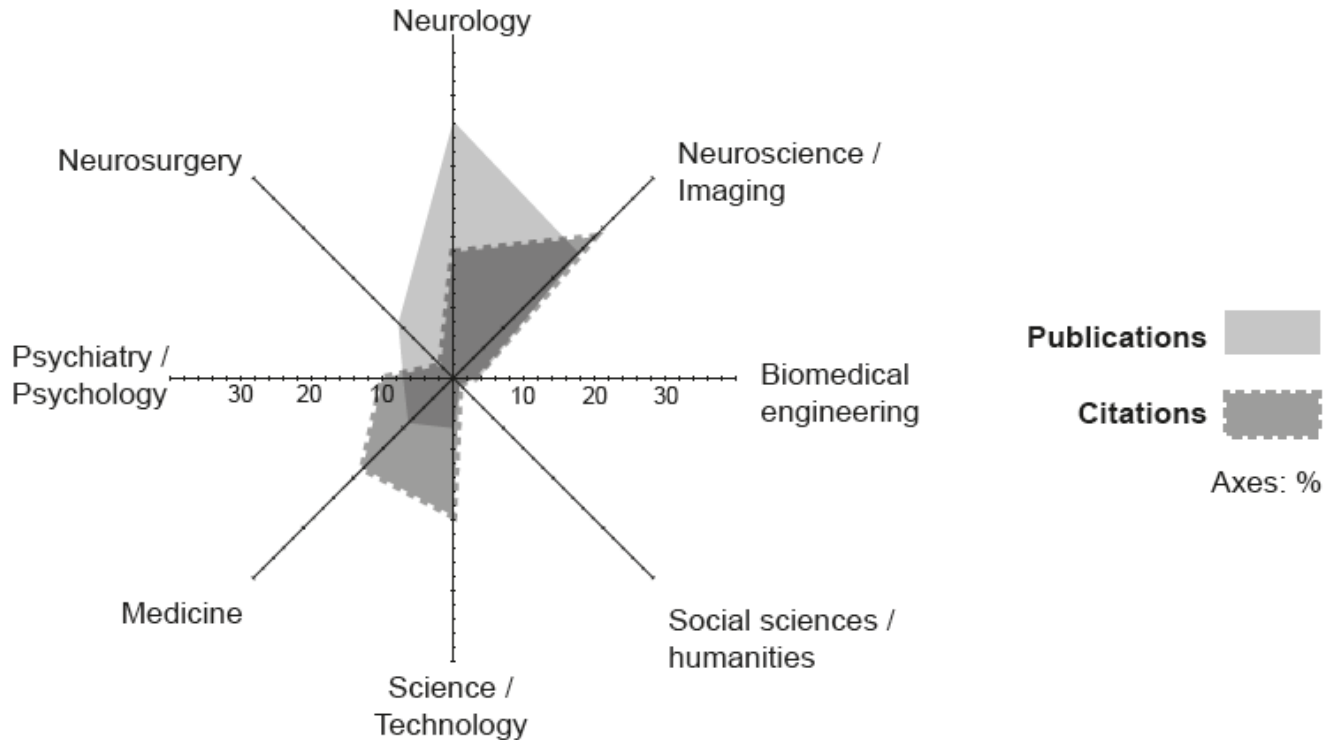




Knowledge transfer

DBS-research is noticed in a broad spectrum of disciplines.

a)

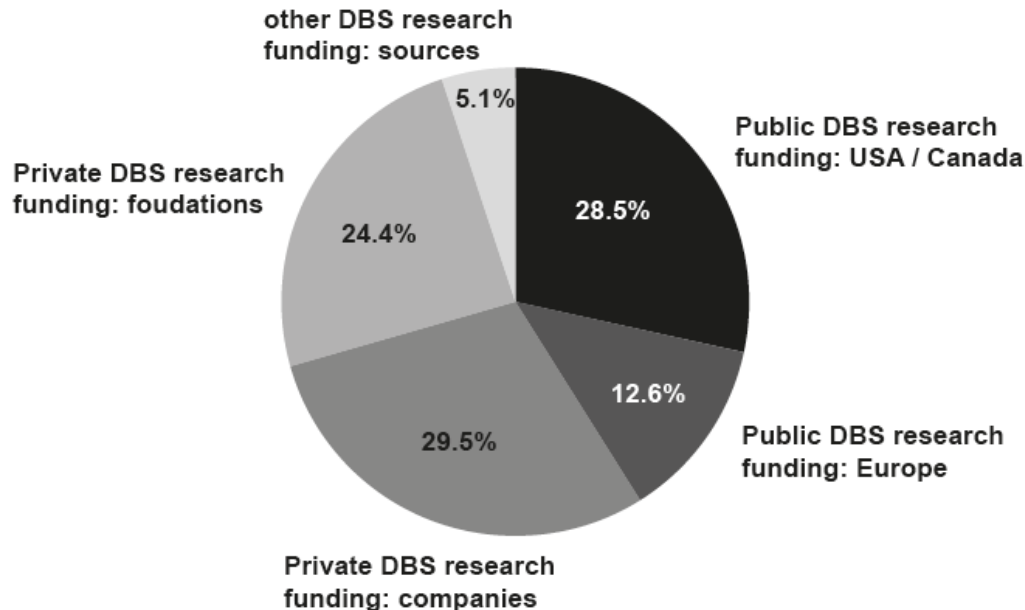




Funding

More than half of DBS research funding emerges from private sources (this data may be incomplete). 19.8% of all US-Papers mention public funding by governmental institutions, whereas only 5.3% of the European DBS papers mention a public source

b)





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General expert opinions



The future of lesion procedures

Experts believe that lesions still can be acceptable in some places but they are unsure whether the practice will survive.

	strongly disagree	disagree	indifferent	agree	strongly agree
Lesions are part of the past, they should not be performed any more	14.2%	37.7%	18.9%	19.8%	9.4%
It's acceptable to offer lesions to patients who do not have a health assurance that will pay for the following costs of DBS and who cannot pay them on their own.	25.7%	20.0%	19.0%	26.7%	8.6%
Lesioning may be acceptable in some cases only if noninvasive methods (e.g. gamma knife) are used.	12.3%	30.2%	33.0%	22.6%	1.9%
It's acceptable to offer lesions to patients who probably will not comply with postoperative care.	4.8%	21.0%	22.9%	44.8%	6.7%
I expect that soon there won't be experts who master lesion procedures.	1.0%	24.8%	27.6%	39.0%	7.6%
It's acceptable to offer lesions in poorer countries if DBS is too expensive.	4.7%	17.0%	17.0%	46.2%	15.1%
For some patients, lesions may be a valid alternative to DBS.	7.5%	5.7%	9.4%	64.2%	13.2%



DBS in movement disorders

Experts believe that DBS in movement disorders is safe and should no longer be considered as a “last resort” treatment. Rather, patients should be able to receive the treatment earlier.

	strongly disagree	disagree	indifferent	agree	strongly agree
DBS surgery has a high risk of complications.	20.8%	51.9%	9.4%	15.1%	2.8%
DBS in movement disorders is still a last resort treatment.	19.8%	47.2%	17.0%	14.2%	1.9%
DBS is a completely reversible procedure.	2.8%	37.7%	17.0%	38.7%	3.8%
DBS in PD is more cost-effective than medication.	2.8%	17.0%	33.0%	40.6%	6.6%
Patients with movement disorders should be able to obtain DBS even when the disease is still manageable by medication.	0.0%	18.9%	20.8%	49.1%	11.3%
DBS should be offered only in large centers.	1.0%	6.7%	16.2%	57.1%	19.0%
More patients should have the opportunity to obtain DBS.	0.0%	1.9%	15.1%	55.7%	27.4%
DBS in movement disorders allows for a better management of disease symptoms than medication alone.	0.0%	1.9%	6.6%	39.6%	51.9%



DBS in general

Experts believe that DBS is a promising therapeutic approach for various neurological and psychiatric diseases. They also believe that economic interests drive the expansion of the indication spectrum.

	strongly disagree	disagree	indifferent	agree	strongly agree
I have a bad feeling when I learn about the increasing number of possible DBS applications.	26.5%	45.1%	18.6%	8.8%	1.0%
There is an economic interest to offer DBS as a novel therapeutic approach for other diseases than movement disorders.	4.0%	7.9%	22.8%	55.4%	9.9%
DBS will allow us to understand the neurological basis of psychiatric diseases.	0.0%	3.9%	28.4%	45.1%	22.5%
DBS will be an option for the treatment of severe, otherwise untreatable psychiatric diseases.	0.0%	0.0%	23.5%	56.9%	19.6%
DBS has the potential to substantially improve our therapeutic spectrum for various diseases.	0.0%	0.0%	5.0%	62.4%	32.7%



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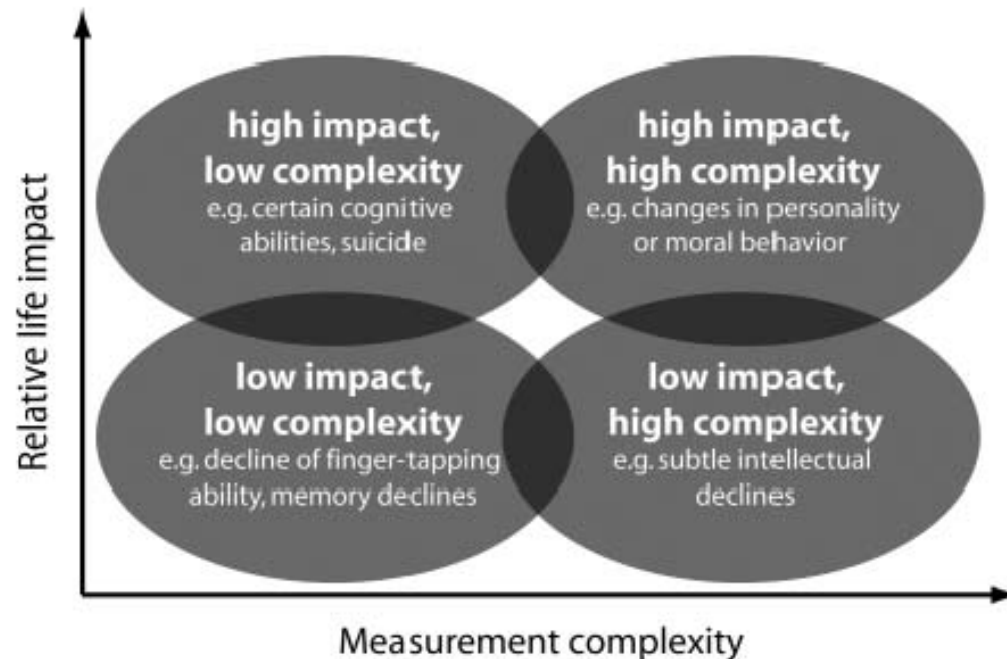
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Recommendations for an ethical future of DBS



Intervention dimension

There is room for improvement on all stages of the intervention process: Information – Decision making – Procedure – Follow-up





Institution dimension

DBS aligns with a fundamental change of understanding various “brain-based” diseases. The side effects of this “re-focusing” with respect to various aspects have to be evaluated carefully:

- Who is involved in (future) treatments?
- Who are the “winners” and “losers” in institutional change?
- Who is paying for research and (later) for treatment?
- What are the effects of single-case success on patients with diseases with high prevalence (depression, obesity)?
- ...



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Thank you!