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S. Kovac, G. Möddel, J. Reinholz, A. V. Alexopoulou, T. Syed, M. Z. Koubeissi, S. U. Schuele, Tara T. Lineweaver, R. M. Busch, and T. Loddenkemper

## **Visual naming performance after ATL resection: Impact of atypical language dominance**

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### **Abstract**

#### **Purpose**

To characterize the interaction between language dominance and lateralization of the epileptic focus for pre- and postoperative Boston Naming Test (BNT) performance in patients undergoing anterior temporal lobectomy (ATL).

#### **Methods**

Analysis of pre- and postoperative BNT scores depending on lateralization of language as measured by the intracarotid amobarbital procedure (IAP) versus lateralization of the temporal lobe epileptic focus.

#### **Results**

Changes between pre- and postoperative BNT performance depended on epilepsy lateralization (effect size = 0.189) with significant decrease in patients undergoing left ATL. Subgroup analysis in these showed that postoperative decline in BNT scores was significant in patients with atypical (n = 14; p < 0.05), but did not reach statistical significance in patients with left language dominance (n = 36; p = 0.09). Chi-square test revealed a trend of higher proportions of patients experiencing significant postsurgical deterioration in naming performance in atypical (57.1%) as compared to left language dominance (30.6%; p = 0.082). Surgical failure was also associated with greater decline of BNT scores and was more common in atypical than in left language dominant patients ( $\chi^2$  (1, n = 98) = 4.62, p = 0.032). Age of onset, duration of epilepsy, and seizure frequency had no impact on changes in BNT performance.

#### **Conclusion**

Atypical language dominance is a predictor of change in visual naming performance after left ATL and may also impact postsurgical seizure control. This should be considered when counseling surgical candidates.

### **1. Introduction**

Neuropsychological outcome after resective surgery for intractable temporal lobe epilepsy (TLE) has been investigated in detail over the last decades. There is a link between impairment on visually based object naming tests and left dominant temporal lobe epilepsy and left dominant temporal lobe resection (Busch et al., 2005, Busch et al., 2009, Chelune et al., 1991, Davies et al., 1998, Davies et al., 1995, Hermann et al., 1997 and Hermann et al., 1999). Previous studies

on Boston Naming Test (BNT) score changes and naming decline after left temporal resection have focused on left language dominant patients and excluded patients with atypical language dominance (Davies, Risse, & Gates, 2005). Confrontational naming requires linking visual semantic information with phonological representations and some of the required networks are in the temporal lobe (Luders et al., 1991). The aim of this study was to characterize the impact of atypical language dominance on BNT performance in patients with intractable TLE before and after anterior temporal lobectomy (ATL).

## **2. Methods**

### **2.1. Patients**

We reviewed the medical records of all patients who underwent the intracarotid amobarbital procedure (IAP) for surgical evaluation of intractable TLE between 1996 and 2001. During that time period, IAP was performed in ~80% of patients undergoing surgery for TLE. We included patients with unilateral TLE according to video-EEG monitoring, complete information regarding language lateralization as determined by the intracarotid amobarbital procedure (IAP), pre- and postoperative BNT, and high resolution brain MRI, irrespective of language lateralization and type of lesion. 101 patients had TLE, 50 had left TLE and 51 had right TLE. Among patients with left TLE, 36 were left hemisphere dominant for language, whereas 14 were atypical language dominant. Only three patients in the right TLE group had atypical language dominance; the other 48 right TLE patients were left hemisphere dominant for language. Therefore subgroup analysis on language lateralization and BNT scores was not performed in right TLE.

Postsurgical assessment of the resected tissue confirmed hippocampal sclerosis in 58 cases (47 cases isolated and 11 cases of dual pathology), 11 cortical dysplasias, two cavernous angiomas, and five low grade tumors. In 24 patients, non-specific gliosis was found in the resected tissue. Pathology data was missing for another patient whose MRI was suggestive of hippocampal sclerosis. The interval between the pre- and postoperative BNT assessment was  $10.3 \pm 3.3$  month (mean  $\pm$  SD). We screened the medical records for postsurgical follow-up in 2009. Data ranged from 5 months to 12 years ( $57.5 \pm 4$  months) and was available for 98 patients. Within our cohort, 80% of patients were free of disabling seizures (Engel I), with 50% being completely seizure free (Engel Ia) after surgery. 7% had ongoing severe seizures (Engel IV). Surgical failure was defined as Engel score II–IV.

## **2.2. Comparison between left and atypical language dominance**

Patients suffering from left TLE did not differ in their demographic, clinical and neuropsychological profile with regards to factors that are known to impact on naming performance (Bell and Davies, 1998, Randolph et al., 1999 and Ruff et al., 2007).

Left handedness as was found to be significantly higher in patients with atypical compared to left language dominance ( $F(1) = 4.66$ ;  $p < 0.05$ ; Table 1).

## **2.3. Visual naming**

All patients completed the 60-item BNT before and after ATL. In addition to examining raw scores on this measure, we classified patients into those that improved in postoperative BNT performance (increase of postoperative score  $\geq 5$ ) and those that deteriorated in naming performance after surgery (decrease of postoperative score  $\geq 5$ ) based on the reliable change

index (RCI) scores offered by Sawrie, Chelune, Naugle, and Luders (1996). These RCIs cut-off scores not only take into account regression to the mean and practice effects associated with retesting, but also account for changes in BNT scores that may result from having epilepsy (without undergoing surgery). Thus, they allowed the effect of surgery on BNT performance to be isolated from these possible confounding factors.

#### **2.4. Wada testing**

Angiography was performed using standard catheter insertion techniques (Moddel, Lineweaver, Schuele, Reinholz, & Loddenkemper, 2009). Amobarbital ( $n = 94$ ) or methohexital ( $n = 7$ ) was given by intracarotid hand push injection.

#### **2.5. Language lateralization**

Language lateralization was quantified based on speech arrest times. We dichotomized patients into left or atypical, i.e. bilateral or right language dominance. For lateralizing language three lateralization measures were defined: (1) the absolute duration of the speech arrest after left and right intracarotid barbiturate injection being greater than 60 s on one side and less than 60 s on the other, (2) the difference between left and right injection speech arrest times ( $t_L - t_R$ ) with a cut-off of 30 s; and (3) the laterality index (LI). The LI was calculated by the difference between speech arrest times after left and right injections, divided by the sum of speech arrest times after left and right injection  $[(t_L - t_R)/(t_L + t_R)]$ , with a cut-off of 0.5. Left or right language dominance was classified if two of three of these lateralization criteria were met. Bilateral language dominance was classified in the remaining patients with bilateral dependent (BD) language

dominance showing absolute speech arrests times of  $\geq 60$  s and bilateral-independent (BI) of  $< 60$  s after either injection ( Benbadis et al., 1995 and Moddel et al., 2009).

## **2.6. Seizure frequency**

Preoperative seizure frequency was classified in a grading system ranging from 1 to 7 (1: one seizure per month, 2: between one seizure per month and one seizure per week, 3: one to two seizures per week, 4: three to six seizures per week, 5: one to two seizures per day, 6: three to ten seizures per day, 7: more than ten seizures per day). Seizure frequency was available for all except one patient.

## **2.7. Statistical analyses**

We used SPSS 15.0 (Chicago, IL, USA) for Student's *t*-test, Chi-square test, and repeated measures ANOVA, and Statistica 8.0 (Statsoft, Inc., Tulsa, OK) for ANCOVA models. Effect sizes for ANOVA and ANCOVA models were estimated using partial eta-squared. For all statistical comparisons, a significance level of 0.05 was accepted. If not indicated, data is given as mean  $\pm$  standard error of mean.

## **3. Results**

### **3.1. BNT change and epilepsy lateralization**

ANCOVA modelling with postoperative BNT performance as the dependent variable, preoperative BNT performance as a covariate, and epilepsy lateralization as the between-group factor revealed that change between pre- and postoperative BNT performance significantly depended on epilepsy lateralization ( $F(1,98) = 22.9$ ;  $p < 0.001$ ; effect size = 0.189). Post hoc

testing revealed that performance in the BNT decreased by approximately three points after surgery in patients suffering from left TLE ( $t(49) = 2.66$ ;  $p < 0.01$ ), whereas performance improved by approximately two points after right ATL ( $t(50) = -4.22$ ;  $p < 0.01$ ; Table 2; Fig. 1A). In both subgroups, the mean change in confrontation naming performance differed significantly from zero (left:  $-3.24 \pm 1.22$ ;  $p < 0.01$ ; right:  $2.00 \pm 0.49$ ;  $p < 0.01$ ). Repeated measures ANOVA produced the same results on reanalysis.

### **3.2. BNT change and language dominance**

Due to the small number of atypical language dominant patients in the right TLE group, the analysis of the impact of language dominance on BNT was restricted to the left TLE group only.

Prior to surgery, left TLE patients performed similarly on the BNT, regardless of whether their language was lateralized to the left hemisphere ( $n = 36$ ) or they displayed atypical language dominance ( $n = 14$ ;  $t(48) = 0.51$ ; ns).

BNT performance in left language dominant patients showed a downward trend ( $t(35) = 1.77$ ;  $p = 0.09$ ) whereas BNT performance of patients classified as atypical language dominant deteriorated significantly after left temporal lobe surgery ( $t(13) = 2.19$ ;  $p = 0.047$ ; Table 2; Fig. 1B and C). Despite a trend of younger age in atypical language dominant patients, age did not influence findings since ANCOVA including age was not significant ( $p = 0.21$ ).

Age of onset, duration of epilepsy and seizure frequency were entered individually, simultaneously, and as interaction terms into the ANCOVA model in order to test for their impact on change in naming performance. Neither of these variables were found to be statistically significant ( $p > 0.05$ ).

For further analysis of the impact of language dominance on BNT performance after



surgery, we used RCI cut-off scores to assign patients to one of three groups: improvement, decline, or no change in naming performance after temporal lobectomy. Relevant decline in postsurgical BNT performance was seen in 30.6% of patients with left language dominance and 57.1% of patients with atypical language dominance, indicating a trend towards a higher risk of naming decline in patients with atypical language dominance after resection of the left temporal lobe ( $\chi^2 (1, n = 50) = 3.02, p = 0.082$ , Fig. 2A and B). In RCI cutoff analysis, univariate and multivariable logistic regression were used to assess the impact of age of onset, duration of epilepsy and seizure frequency on BNT change in left TLE patients. Neither of these predictors attained significance either individually, in combination, or in interaction terms.

### **3.3. BNT change and surgical outcome**

Analysis of BNT score change as a function of seizure outcome classified by Engel's criteria revealed that patients who continued to have seizures after surgery (Engel II–IV) demonstrated greater declines in BNT score following surgery compared with those who were free of disabling seizures (Engel I), irrespective of the side of seizure focus ( $n = 98; t(17.4) = -2.40; p < 0.05$ ). Surgical failure was associated with atypical language dominance ( $\chi^2 (1, n = 98) = 4.62, p < 0.05$ ). Surgical failure was prevalent in 50% left TLE patients with atypical language dominance compared to 27.3% in left language dominant patients experiencing a significant decrease in naming performance. Due to small numbers further subgroup analysis of surgical outcome was not performed.

## **4. Discussion**

### **4.1. Summary**

Consistent with prior reports, we found a significant relationship between pre- and postoperative BNT performance and side of epilepsy. Left ATL was associated with a decline in visual confrontation naming after surgery, whereas patients with right ATL improved. Although patients with both left and atypical language representation as assessed by the IAP had a decline in naming after left-sided resection, the risk of significant deterioration in naming ability was unexpectedly higher in left ATL patients who had atypical language representation. Analysis of surgical outcome revealed that patients with atypical language dominance had poorer seizure outcome and demonstrated greater naming decline following surgery.

#### **4.2. BNT performance**

Studies of performance on naming tests have demonstrated impairment on visually based object naming tests in patients with left dominant TLE, highlighting the importance of left temporal lobe structures in visual naming (Busch et al., 2005, Busch et al., 2009, Chelune et al., 1991, Davies et al., 1995, Davies et al., 1998, Hermann et al., 1997, Hermann et al., 1999 and Sawrie et al., 2000). This impairment was closely linked to age of onset and duration of epilepsy, factors that have been taken into account in our analysis (Bell et al., 2002 and Schwarz et al., 2005). However, this relation was not seen in our study. Right temporal lobe resection has been associated with postoperative improvement in memory function (Baxendale, Thompson, & Duncan, 2008) and moreover of BNT scores (Ruff et al., 2007). Our results regarding right ATL are similar to those of Ruff et al. That is, our right TLE group also showed mild post-surgical BNT improvement.

#### **4.3. BNT performance in atypical language dominance**

If atypical language dominance indicates partial reorganization of naming areas to the contralateral hemisphere, then it should be associated with better outcome after resection of left hemispheric structures. Instead, our results suggest that even in patients with atypical language lateralization, networks relevant for naming are present in the left hemisphere posing a higher risk for deterioration after surgical resection compared to patients with left language dominance. Evidence from direct cortical stimulation and IAP studies reveals that atypical language lateralization represents a spectrum of language organizations that depends on left hemisphere structures (Moddel et al., 2009 and Wyllie et al., 1990). In parallel with these findings, we found that naming in patients with atypical language representation patients seemed to depend on left hemispheric function.

Supporting our findings, intrahemispheric reorganization of visual naming sites have been described before (Hamberger and Seidel, 2009 and Hamberger et al., 2007) and neocortical structures rather than the hippocampal volumes were linked to visual naming performance (Seidenberg, Geary, & Hermann, 2005). Very few studies have addressed naming performance in patients with atypical language dominance. One study showed that bilateral (atypical) language representation was associated with more than one non-contiguous language area in the left temporal lobe (Jabbour et al., 2004). Mapping of language function in this study revealed that in both bilateral and left dominant language representation, language areas were located between three and nine cm from the left temporal tip. Standard left dominant temporal lobe resection is performed within a margin of less than five cm. Four patients in the study mentioned above had a language area anterior to five cm, with three of them revealing atypical language dominance. In line with this set of findings and our results, left-handedness, often indicating atypical language dominance, has been identified as one marker of the presence of essential

language areas in the anterior regions of the temporal lobe (1.5–3.5 cm from the temporal tip) (Schwartz, Devinsky, Doyle, & Perrine, 1998).

Anterior displacement of language areas may be one explanation for more prevalent decline in BNT performance after left ATL in the group of atypical language dominant patients in our cohort. In line with that argument, using a combination of fMRI and tractography, one study demonstrated a structural reorganization of white matter tracts that reflects the altered functional language lateralization in left TLE patients (Powell et al., 2007). Thus, atypical language dominance may reflect altered structural connectivity that may account for more extensive involvement of brain areas and thus larger epileptogenic focus. Altered connectivity may be an explanation for a poorer seizure outcome after resection in atypical language dominant patients in our cohort.

Interictal and also seizure driven functional language organization has been reported in previous studies (Helmstaedter et al., 2006 and Janszky et al., 2003).

Our results need to be interpreted in the setting of the retrospective study design. Subgroup analysis of atypical language dominance, i.e. right dominant vs. bilateral dependent and bilateral independent patients could not be performed due to small proportion of atypical language dominant patients in our cohort. Retrospective data analysis did not allow us to utilize more comprehensive clinical language assessment protocols (Weber et al., 2006), and language lateralization was limited to assessment based on speech arrest only. Language lateralization assessed by speech arrest has been found to differ from language lateralization assessment by comprehensive language assessment (Benbadis et al., 1998). Since IAP procedures can vary from centre to centre, findings of this study may not generalize well to other centres that are using different IAP procedures for evaluation of language dominance.

## 5. Conclusion

In line with previous reports, significant decline in naming performance is associated with left temporal lobe resection and is observed in 40% of patients. Unexpectedly, atypical language dominance is associated with a higher risk of visual naming performance decline and a higher propensity of surgical failure after ATL compared to left hemisphere language dominance.

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Table 1.

Demographics, clinical and neuropsychological data.

	LTLE			RTLE
	Left language dominant patients	Atypical language dominant patients	<i>p</i> ( <i>T</i> / <i>df</i> )	All
Age in years	31.9 (11.9)	29.6 (8.2)	0.525 (0.64/48)	32.6 (12.3)
Age at Seizure Onset in years	14.8 (13.1)	12.6 (13.2)	0.609 (0.52/48)	13.1 (11.1)
Duration of Epilepsy	17.4 (11.5)	17.4 (10.8)	0.991 (0.01/48)	20.2 (12.4)
Interval between pre- and postoperative NPA in months	10.9 (3.6)	10.7 (2.7)	0.849 (0.19/48)	9.8 (3.2)
Education in years	12.8 (2.0)	12.6 (1.2)	0.683 (0.44/48)	12.6 (2.2)
Full Scale IQ <sup>1</sup>	93.2 (12.6)	93.1 (13.3)	0.983 (0.02/40)	89.3 (12.4)
Verbal IQ <sup>1</sup>	90.8 (11.6)	90.0 (12.5)	0.884 (0.15/31)	90.0 (13.2)
Performance IQ <sup>1</sup>	96.1 (14.6)	97.6 (17.4)	0.796 (-0.26/39)	90.7 (12.7)
Lesion on MRI <sup>2</sup>	<i>n</i> = 31/36	<i>n</i> = 9/14	0.083 (3.00/1)	<i>n</i> = 46/51
Left handed patients <sup>3</sup>	<i>n</i> = 2/32	<i>n</i> = 4/10	0.031* (4.66/1)	<i>n</i> = 4/51

IQ: intelligence quotient (Wechsler scores); NPA: [neuropsychological assessment](#); all data except from <sup>2</sup> given as mean (SD). <sup>1</sup>Full Scale IQ was available from 89, Performance IQ from 86 and Verbal IQ from 67 patients all other demographics were available from all 101 patients. <sup>3</sup>Handedness was available from 99 patients.

\*Significant ( $p < 0.05$ ).

Table 2.

Performance on BNT according to language dominance and side of epilepsy surgery; BNT 1 and BNT 2: mean  $\pm$  SEM.

	All patients		L TLE	
	L TLE <i>n</i> = 50	R TLE <i>n</i> = 51	Left language dominant <i>n</i> = 36	Atypical language dominant <i>n</i> = 14
BNT 1	44.7 $\pm$ 1.2	47.5 $\pm$ 1.0	45.1 $\pm$ 1.4	43.7 $\pm$ 2.4
BNT 2	41.5 $\pm$ 1.3	49.6 $\pm$ 1.1	42.5 $\pm$ 1.5	38.7 $\pm$ 2.6
Significance BNT 1 vs. BNT 2 ( <i>T</i> , <i>df</i> )	<i>p</i> = 0.010 (2.66/49)	<i>p</i> = 0.000 (-4.22/50)	<i>p</i> = 0.085 (1.77/35)	<i>p</i> = 0.047 (2.19/13)

L TLE: left temporal lobe R TLE: right temporal lobe.



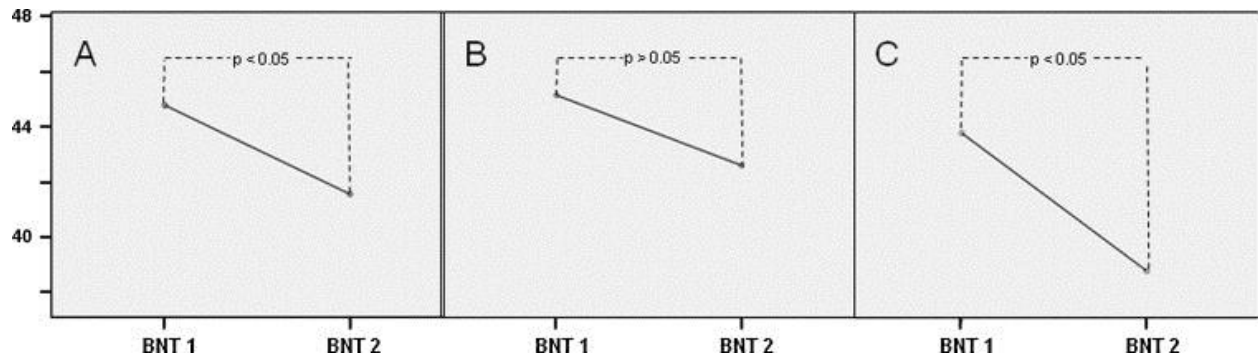


Figure 1 Pre- and postoperative BNT performance in left temporal lobe epilepsy patients. BNT 1: preoperative BNT score; BNT 2: postoperative BNT score. A: overall analysis; B: left language dominant patients; C: atypical language dominant patients.

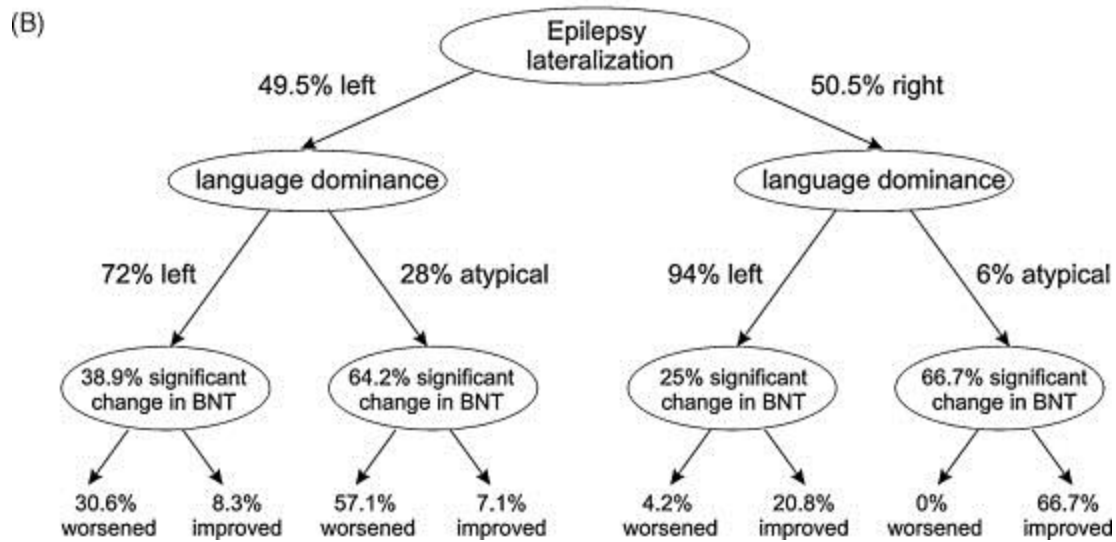
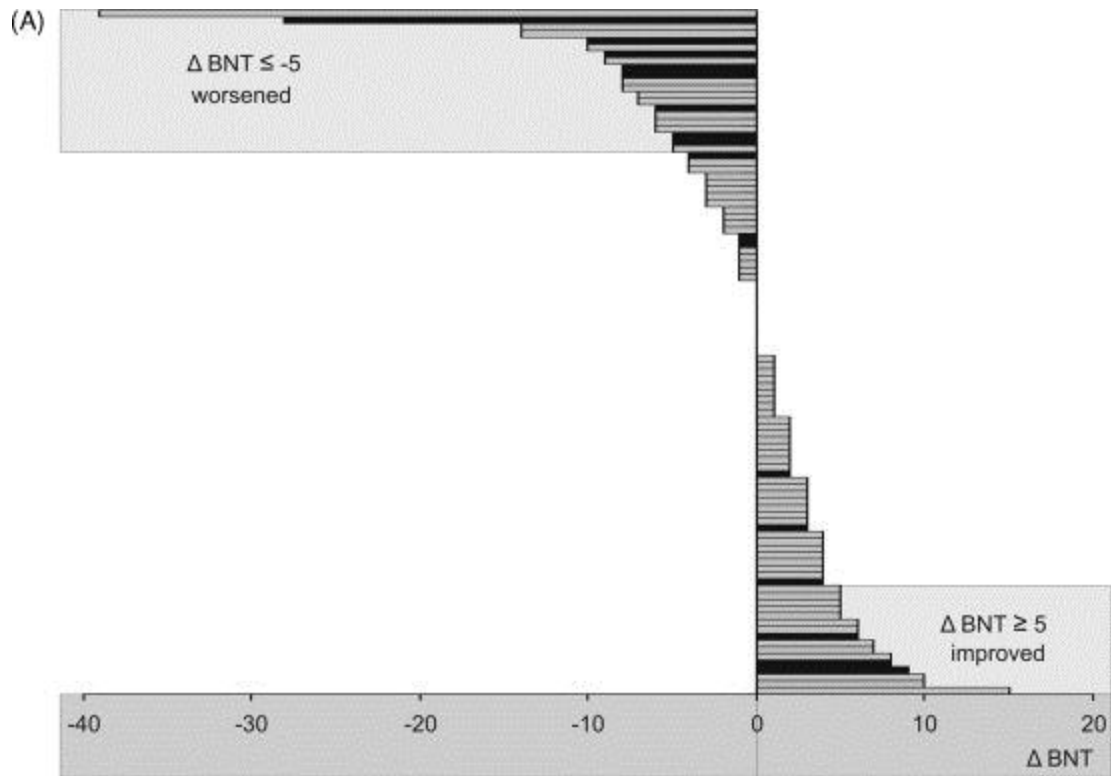


Figure 2 (A) Change in BNT raw scores after surgery ( $\Delta$  BNT). Horizontal bars represent single changes in BNT performance. Grey background indicates cut-off to significant improvement (bottom of the graph) or significant decline (top of the graph) in BNT performance. Black bars represent patients with atypical language dominance. (B) Flow chart of significant improvement and deterioration on postoperative BNT-performance dependent on epilepsy lateralization and language dominance.