

# EEG spectral power and negative symptoms in at-risk individuals predict transition to psychosis

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## Abstract

**Objective:** EEG power in the delta, theta and beta1 bands has been shown to be positively correlated with negative symptoms in first episode psychotic patients. The present study investigates this correlation in an “at risk mental state for psychosis” (ARMS) with the aim to improve prediction of transition to psychosis.

Gelöscht: Introduction

**Methods:** Thirteen ARMS patients with later transition to psychosis (ARMS-T) and fifteen without (follow-up period of at least 4 years) (ARMS-NT) were investigated using spectral resting EEG data (of 8 electrodes over the fronto-central scalp area placed according to the 10 – 20 system) and summary score of the Scale for the Assessment of Negative Symptoms (SANS).

Linear regressions were used to evaluate the correlation of SANS and EEG power in seven bands (delta, theta, alpha1, alpha2, beta1, beta2, beta3) in both ARMS groups and logistic regressions were used to predict transition to psychosis. Potentially confounding factors were controlled.

**Results:** ARMS-T and ARMS-NT showed differential correlations of EEG power and SANS in delta, theta, and beta1 bands ( $p < 0.05$ ): ARMS-T showed positive and ARMS-NT negative correlations. Logistic regressions showed that neither SANS score nor EEG spectral power alone predicted transition to psychosis. However, SANS score in combination with power in the delta, theta, beta1, and beta2 bands, respectively, predicted transition significantly ( $p < 0.03$ ).

**Limitations:** The number of subjects is relatively small. The difference in age of both study groups might be considered as a further limitation even though age had no effect on the results according to confounder analysis.

**Conclusions:** ARMS-T and ARMS-NT show differential correlations of SANS summary score and EEG power in delta, theta, and beta bands. Prediction of transition to psychosis is possible using combined information from a negative symptom scale and EEG spectral data.

**Keywords:** schizophrenia, prediction, at risk mental state, quantitative EEG, negative symptoms, Fast Fourier Transform (FFT)

## Introduction

Ultra high risk studies aim at improving the early detection of psychosis in order to provide earlier and more efficient treatment to patients suffering from psychosis.<sup>1-2</sup> Predominant criteria utilized to date are attenuated (sub-threshold) psychotic symptoms of brief limited psychotic episodes, genetic risk, and social decline.<sup>3</sup> However, not all patients identified as being in an “at risk mental state for psychosis” (ARMS) by these criteria develop psychosis. The differentiation between ARMS patients who will make the transition to psychosis (ARMS-T) and ARMS patients who will not develop the disease (ARMS-NT) is of crucial importance. Recently reported transition-to-psychosis rates from our group were 34%<sup>4</sup> and ranged from 9% to 54% in other high risk studies (see review by Olsen et al.)<sup>5</sup>. Other recent studies suggest transition rates of about 15%.<sup>6-7</sup> Thus, current criteria result in many ‘false positives’, which puts unnecessary burden on patients. Supplementary to the criteria of Yung et al.<sup>3</sup> other risk factors have been detected that can potentially improve the identification of ARMS-T patients.

- ARMS-T patients are more severely impaired in certain neuropsychological domains compared to ARMS-NT patients and can be discriminated based on cognitive performances.<sup>8</sup> For example, in a recent study of Riecher-Rössler et al.<sup>4</sup> neuropsychological data were combined with psychopathological ratings (i.e., Brief Psychiatric Rating Scale, BPRS)<sup>9</sup> and Scale for the Assessment of Negative Symptoms (SANS)<sup>10</sup> to enhance prediction of transition to psychosis.
- Neuroimaging studies (for review Wood et al.)<sup>11</sup> detected structural changes in ARMS patients using structural magnetic resonance imaging.<sup>12</sup> Koutsouleris et al.<sup>13</sup> were able to classify ARMS-T patients with an accuracy of 88% using a multivariate whole-brain technique.
- Evoked potential studies have been conducted in ARMS patients (e.g.<sup>14-16</sup>). However, so far only Brockhaus-Dumke et al.<sup>17</sup> compared ARMS-T with ARMS-NT. Their

results indicate that N100 suppression evaluated in a double click paradigm is significantly reduced in ARMS-T ( $p < 0.05$ ), first episode (FE,  $p < 0.001$ ), as well as chronic patients ( $p < 0.001$ ) compared to healthy controls but not ARMS-NT ( $p = 0.052$ ). However, ARMS-T and ARMS-NT did not differ on any of the studied parameters.

- Moreover, conventionally (non quantitatively) analyzed resting EEG was shown to increase the specificity of prediction of transition to psychosis in ARMS from 59% to 73%.<sup>18</sup>

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The present study tests the hypothesis that a combination of negative symptoms and spectral power of resting EEG increases predictive accuracy of transition to psychosis in ARMS patients. This hypothesis originates from the observation that negative symptoms and quantitative EEG (qEEG) spectral power are correlated in different types of medicated and unmedicated schizophrenic patients.<sup>19-27</sup> Moreover, a recent study by our group<sup>28</sup> showed that negative symptoms are positively correlated with qEEG absolute power in delta (0.5-4 Hz), theta (4-8 Hz) and beta1 (12-15 Hz) bands in the first episode (FE) of schizophrenia in neuroleptic-naïve patients. Presence of these correlations in neuroleptic naïve FE patients is a first requirement for the combination of negative symptoms with qEEG findings in ARMS patients to be a valid predictor for transition to psychosis. We expected to find correlations in the group of ARMS-T patients similar to those found in FE patients. A further requirement for the prediction of transition is absence of these correlations in ARMS-NT patients.

Thus, the objectives of the current study are to examine 1) whether the correlation of negative symptoms and EEG spectral power in ARMS-T patients is similar to that observed in the previously analyzed FE patients, but absent or different in ARMS-NT patients, and 2) whether it is possible to improve prediction of transition to psychosis in ARMS patients based on an increase of power in delta, theta, and beta1 frequency bands in combination with a negative symptom score (SANS).

## Methods

### Subjects

Data from 13 ARMS-T and 15 ARMS-NT patients from the FEPSY (Early Detection of Psychosis) Clinic at the University Psychiatric Outpatient Department, Basel, Switzerland were analyzed. Baseline data including BPRS, SANS and EEG were collected at patients' first intake into clinic. Patients were then regularly followed-up. Criteria for ARMS and transition to psychosis were defined according to Yung et al.<sup>3</sup> and are shown in Table 1. The detailed screening process has been described elsewhere.<sup>4,29</sup>

--- Insert Table 1 about here ---

Exclusion criteria were age younger than 18 years, insufficient knowledge of German, IQ <70, previous episode of schizophrenic psychosis (treated with major tranquillizers for >3 weeks), psychosis clearly due to organic reasons or substance abuse, or psychotic symptoms within a clearly diagnosed depression or borderline personality disorder.

After complete description of the study to the subjects, written informed consent was obtained from all participants. The study was approved by the local ethics committee (Ethikkommission beider Basel, EKBB). A further condition for ARMS-NT patients was a follow-up period of at least four years. Four patients were on low dose neuroleptics (chloprothixen) prescribed for sedation, six patients were treated with antidepressive drugs (escitalopram, citalopram, paroxetine, sertraline, fluoxetine, venlafaxin) and three patients were on benzodiazepines (lorazepam, zolpidem). The patients' mean age was 25.7 (SD 7.6), 18 subjects were male and 10 were female.

## **Psychopathological ratings**

Patients were rated at study entry (baseline) with the Scale for the Assessment of Negative Symptoms (SANS)<sup>10</sup> which consists of five subscales that evaluate aspects of negative symptoms (alogia, affective blunting, avolition-apathy, anhedonia-asociality, and attentional impairment). We calculated SANS summary score as described by Andreasen.<sup>30</sup> Mean SANS summary score was 8.4 (SD 5.5, range 0-19). The variable was normally distributed.

## **EEG data acquisition**

Only patients with a digitally recorded EEG at study entry (“baseline”) were included. Routine EEG recordings of about 20 min duration were performed in a quiet room with closed eyes. Patients were instructed by the technicians to open eyes about every third minute for a period of five to six seconds. Additional open eyes segments were required if the patient showed signs of sleepiness.

EEG data were digitally recorded using 21 gold cup electrodes placed according to the international 10/20 system. Impedances were kept below 5 k $\Omega$ . Amplifiers were calibrated using a 50  $\mu$ V square pulse. Sampling frequency was 250 Hz. All channels were referenced to linked ears. EEGs were recorded with Alliance Works for Windows NT<sup>TM</sup> (Nicolet Biomedical Inc., Madison, Wisconsin). Raw EEG data were converted to European Data Format with Nicolet Data Converter (Nicolet Biomedical Inc., Madison, Wisconsin). Data were then read into Brain Vision Analyzer<sup>®</sup> software (BVA; Brain Products GmbH, Munich, Germany). We selected 19 electrodes (Fp1, Fp2, F3, F4, C3, C4, P3, P4, O1, O2, F7, F8, T3, T4, T5, T6, Fz, Cz and Pz), recalculated the reference to average and set the high- and low

pass (Butterworth) filters to 0.5–120 Hz. We then removed eyes open sequences that had been marked by the technicians during the recording with the tool “Segmentation” of BVA.

### **Artefact rejection**

To ensure high validity of the analysis Boutros et al.<sup>31</sup> recommend a minimum of 25 artefact free segments of 2 seconds duration (see also Lund et al.).<sup>32</sup> To conserve a maximum of EEG recording we used a semi-automatic standard operating procedure (SOP) to remove artefacts. The procedure consisted of three steps: 1) Continuous data containing obvious artefacts (e.g., electrode artefacts), except for those caused by eye movements, were manually deleted over all electrodes and remaining segments were juxtaposed. 2) In order to remove well defined sources of artefact, an independent component analysis (ICA) was performed with BVA. Once the independent time courses of different brain and artefact sources were extracted from the data, corrected EEG signals were computed by eliminating the contributions of the artefact sources. The ICA has been demonstrated to reliably isolate artefacts due to horizontal and vertical eye movements, heart electrical interference, and to some extent muscle or line noise.<sup>33</sup> 3) In a last step, the already corrected EEG was visually inspected by an experienced neurophysiologist who was blind to the patient’s symptoms and diagnosis. He removed further artefacts not readily removed in steps 1 and 2 from the EEG recording, including muscle, movement and electrode artefacts. Patients with EEGs containing deeper sleep than stage A of Loomis et al.<sup>34</sup> and with EEGs that showed EEG-identifiable pathologies (e.g., generalized epilepsy) were excluded from further analyses. After artefact removal, EEG recordings were divided into segments of two seconds. The remaining EEG recordings had a minimum length of 68 two-second-segments and an average length of 204.5 sec (SD=122).

### **Analysis and statistics**



EEG power for all electrode sites was calculated using Fast Fourier Transform (FFT) (Hanning Window, 20% taper length, 0.5 Hz bins from 0.5 to 30 Hz) implemented in BVA. Data were exported into R-Software<sup>35</sup> for statistical analysis. The FFT output data over the 0.5 Hz bins were combined to delta (0.5–4 Hz), theta (4–8 Hz), alpha1 (8–10 Hz), alpha2 (10–12 Hz), beta1 (12–15 Hz), beta2 (15–25 Hz) and beta3 (25–30 Hz) bands by calculating the mean of the corresponding 0.5 Hz frequency bins. Analyses were performed *a-priori* on average power of the 8 electrode sites used in our previous study,<sup>28</sup> roughly covering the fronto-central half of the scalp (Fp1, F3, C3, Fz, Cz, Fp2, F4, C4). Other locations were not analyzed to minimize type I error. All EEG variables were transformed by natural logarithm to achieve normal distribution.

#### *Correlation of EEG spectral power with SANS scores in ARMS patients*

We performed one general linear regression per EEG band using absolute spectral power as dependent variable. Negative symptom score as well as group (ARMS-T vs. ARMS-NT) and the interaction term of group and negative symptom score were independent variables. We controlled for potential confounders (age, gender, use of benzodiazepines, use of antidepressants, use of low-dose neuroleptics, use of cannabis, and day time of EEG recording) by doing sensitivity analysis, i.e., we inserted the potentially confounding factors one by one into the regression models and checked whether the additional factor had relevant influence on the reported results.

To better illustrate the correlations of power and SANS for each group separately estimates and 95% confidence intervals (CI) were derived from mathematically equivalent stratified linear models with group-specific slopes of the negative symptoms variable (i.e., the respective group-specific terms were obtained by multiplying the original negative symptoms variable with the respective group indicator variable).

To control for interindividual variability in EEG absolute power, we additionally calculated mixed effect models.<sup>36</sup> For every band, power with a resolution of 0.5 Hz was used as dependent variable. Group and SANS score were used as fixed effects as in the general linear regression models. Intercept was used as random effect.

#### *Prediction of transition to psychosis*

To predict transition to psychosis using EEG power and SANS summary score collected at baseline, logistic regression models were calculated. ARMS status (T vs. NT) was used as dependent variable. Negative symptoms and EEG power (as well as the interaction of both variables) were used as independent variables. Finally, optimal cut-off scores for determining sensitivity, specificity, and prediction accuracy were calculated for the logistic regression models.

## Results

### Sample description

Table 2 summarizes characteristics of the studied groups. While ARMS-T and ARMS-NT differed in age ( $p = 0.03$ ) and while EEGs of both groups were recorded at different times of day ( $p = 0.02$ ), no statistical difference could be found in terms of gender, medication, use of cannabis, intensity of negative symptoms, BPRS score and absolute power in different bands.

**Gelöscht:** One patient was excluded due to sleepiness during EEG recording, one due to persistent electrode and movement artifacts.

--- Insert Table 2 about here ---

### Correlation of EEG spectral power with SANS scores in ARMS patients

Table 3 shows results of linear regression models describing the correlation between power in seven frequency bands and negative symptoms (SANS summary score) for both groups (ARMS-T vs. ARMS-NT).

--- Insert Table 3 about here ---

The significant interaction effect between negative symptoms and group indicates that the correlation of negative symptoms and power is differential in ARMS-T and ARMS-NT in the delta ( $p = 0.016$ ), theta ( $p = 0.033$ ), and beta1 ( $p = 0.036$ ) bands.

In ARMS-NT power decreases in these bands with stronger negative symptoms (see estimates and CI in Table 3). In contrast, power of the ARMS-T group increases with stronger negative symptoms in the same bands (see Table 3 and Figure 1).

--- Insert Figure 1 about here ---

#### *Influence of additional variables*

According to sensitivity analysis, none of the potentially confounding factors (including age and daytime of EEG recording) had significant effects on the discussed bands nor did any of them affect the reported results with the exception of intake of benzodiazepines which had a significant effect in the beta2 ( $p = 0.029$ ) and beta3 ( $p = 0.006$ ) bands. We redid the analysis excluding patients on benzodiazepines: The estimates of regression analysis did not relevantly change. A table with results of this sub-analysis can be seen in the supplemental material of the paper.

#### *Further analyses*

The results of the random effect procedure were similar to those of the linear regression models and can be seen in the supplemental material of the paper.

#### *Comparison with first episode patients*

In Figure 2, Spearman rank order correlation coefficients of the current analysis with ARMS patients are displayed together with those of FE patients described in our previous study.<sup>28</sup> The figure shows that FE and ARMS-T patients exhibit a remarkably similar correlation pattern across the entire EEG frequency range. In contrast, the correlation coefficients of ARMS-NT patients are dissimilar and largely in the negative range.

--- Insert Figure 2 about here ---

### **Prediction of transition to psychosis**

Neither SANS nor EEG power scores alone were predictive for transition to psychosis. Results of logistic regression models combining negative symptoms and power are presented in Table 4. The models for the delta, theta, beta1 and beta2 bands had statistically significant predictive power ( $p < 0.05$ ). Within these models the interaction terms (of power and negative symptoms) were significant ( $p < 0.05$ ) as well as the main effects of negative symptoms in models theta, beta1 and beta2.

--- Insert Table 4 about here ---

Table 4 also lists Nagelkerke's  $R^2$  index, optimal probability cut-off scores, the percentage of correctly classified patients, sensitivity and specificity as well as positive and negative predictive values. Best prediction of transition to psychosis was reached with the model combining negative symptoms with power in the theta band with 89% correct classifications. Also the models combining SANS summary score and power in delta, beta1 and beta2 bands showed high predictive accuracy ( $PPC > 0.80$ ).

## Discussion

The first objective was to investigate whether the positive correlations of EEG power in the delta, theta, and beta1 bands with negative symptoms, previously observed in FE patients,<sup>28</sup> are already present before the clinical outbreak (in ARMS-T patients). Direction and degree of these correlations in ARMS-T patients are almost equivalent to those observed in FE patients (see Table 3), although confidence intervals were not clearly in the positive range, probably due to small sample size (N = 13). In ARMS-NT, in contrast, correlations of power in these bands with negative symptoms were clearly negative. Thus, the correlation pattern of ARMS-NT patients was almost a mirror image to that of ARMS-T and FE (see Figure 2). Interaction terms of linear regression analyses indicated that correlations of SANS summary score and power in delta, theta, and beta1 bands differed significantly between ARMS-T and ARMS-NT. Therefore, the first hypothesis of the study, stating that the relationship of negative symptoms and EEG spectral power in ARMS-T patients is similar to that observed in FE, but different in ARMS-NT patients, is largely confirmed.

The second objective was to assess the accuracy of models comprising SANS and qEEG data for prediction of transition of ARMS patients to psychosis. Logistic regression models showed significant predictions for delta, theta, beta1, and surprisingly, for the beta2 band (see Table 4). The models classified transition to psychosis in ARMS patients with an accuracy of over 80%. Therefore, the second hypothesis, stating that it is possible to improve prediction of transition to psychosis in ARMS patients based on power in delta, theta, and beta1 bands in combination with the SANS score, is confirmed. The study suggests that EEG spectral analysis in combination with SANS score might be helpful in predicting transition or non-transition to psychosis in ARMS.

Other applications are conceivable: Currently efforts are made to increasingly base future classification systems of psychoses on biological data.<sup>37</sup> The positive correlations of EEG

power and negative symptoms have been observed in chronic stages of schizophrenia,<sup>20, 23, 25, 27</sup> in FE patients<sup>28</sup> and with the present study also in the prodromal phase of psychosis (ARMS-T) while the same correlations showed sign reversal in a non-psychotic control group (ARMS-NT). QEEG data might, thus, represent an endophenotype<sup>38</sup> associated with behavioral symptoms and could, therefore, be helpful in the differential diagnosis of disorders with negative symptoms.

The associating of higher EEG power in low frequency bands with stronger negative symptoms in schizophrenic patients might be due to a lack of activity in non-motor cortico-basalganglionic-thalamo-cortical circuits as proposed for negative symptom like signs and EEG alterations in Parkinson's disease.<sup>39-41</sup> Speculation about the mechanism underlying the sign reversed correlation in the control group is, however, difficult at this stage.

The current study represents an initial foray into a vital clinical field. Up to now, the question of the specificity of the phenomenon has not been sufficiently investigated and, therefore, studies including different pathological control populations and, additionally, studies with repeated assessment of qEEG in high-risk populations, including patients under the age of 18, to address the question whether EEG alterations represent a state or a trait marker are warranted. Although results are probably not affected by any confounding factors as shown by carefully conducted sensitivity analyses, future studies should make efforts to investigate these phenomena in samples that are comparable in age, which could not be done in the present study.

**Table 1: Criteria for ARMS and transition to psychosis**

<b>Clinical signs</b>	
<b>At Risk Mental State (ARMS)</b>	<p>A) “Attenuated” psychotic symptoms: psychotic symptoms below the transition cut-off (BPRS scales: ratings of hallucinations at 2-3, unusual thought content 3-4, or suspiciousness 3-4) at least several times per week persisting for &gt;1 week; OR</p> <p>B) Brief Limited Intermittent Psychotic Symptoms (BLIPS): psychotic symptoms over the transition cut-off (BPRS scales: hallucinations <math>\geq 4</math>, unusual thought content <math>\geq 5</math>, suspiciousness <math>\geq 5</math>, conceptual disorganization <math>\geq 5</math>), but each symptom lasting &lt;1 week before resolving spontaneously</p> <p>C) Genetic risk category: first or second degree relative with psychotic disorder <i>and</i> at least two further risk factors according to the screening instrument.</p> <p>D) Precondition for all categories: criteria of transition to psychosis remain unfulfilled.</p>
<b>Transition to Psychosis</b>	<p>At least one of the following symptoms:</p> <ul style="list-style-type: none"> <li>• suspiciousness (BPRS <math>\geq 5</math>): subject says others are maliciously talking about him/her, have negative intentions or may induce harm (incidents more than once a week OR partly delusional conviction).</li> <li>• unusual thought content (BPRS <math>\geq 5</math>): full delusion(s) with some preoccupation OR some areas of functioning disrupted (<i>not only</i> ideas of reference/ persecution, unusual beliefs or bizarre ideas without fixed delusional conviction)</li> <li>• hallucinations (BPRS <math>\geq 4</math>): occasional hallucinations OR visual illusions &gt;2 week or with functional impairment (<i>not only</i> hearing of own name, non-verbal acoustic or formless visual hallucinations/illusions).</li> <li>• conceptual disorganization (BPRS <math>\geq 5</math>): speech difficult to understand due to circumstantiality, tangentiality, neologisms, blockings or topic shifts (most of the time OR three to five instances of incoherent phrases).</li> <li>• Symptoms at least several times a week and change in mental state lasting for more than one week.</li> </ul>

Note: BPRS = Brief Psychiatric Rating Scale (Lukoff, 1986)



**Table 2: Demographic and clinical characteristics of ARMS-T vs. ARMS-NT patient groups at baseline**

	ARMS-NT	ARMS-T	Inferential statistic
<b>N</b>	15	13	
<b>Gender (male)</b>	66.6 %	61.5 %	* p = 1
<b>Age, mean (SD) years</b>	23.1 (6.9)	28.7 (7.5)	†W = 50; p = 0.003
<b>High dose neuroleptics</b>	0 %	0 %	Not available
<b>Low dose neuroleptics</b>	13.3 %	15.4 %	* p = 1
<b>Antidepressants</b>	20 %	23.1%	* p = 1
<b>Benzodiazepines</b>	6.7 %	15.4 %	* p = 0.58
<b>Mood stabilizer</b>	0 %	7.7 %	* p = 0.46
<b>Cannabis use</b>			
no	10	8	
less than monthly	0	0	
monthly	1	0	‡χ <sup>2</sup> (df=3) = 0.13; p = 0.73
weekly	2	3	
daily	2	2	
<b>Day time of EEG recording (SD)</b>	10.2 (2.1)	13 (3)	‡W = 49; p = 0.002
<b>SANS global score, mean (SD)</b>	7.6 (5.7)	9.4 (5.3)	§t (df=25.8) = -0.86; p = 0.40
<b>BPRS summary score, mean (SD)</b>	38.6 (10.1)	41.6 (9.1)	§t (df=25.9) = -0.76; p = 0.46
<b>EEG power</b>			
delta (0.5 - 4 Hz, log), mean (SD)	0.13 (0.47)	0.1 (0.38)	§t (df=25.9) = 0.17; p = 0.86
theta (4 - 8 Hz, log), mean (SD)	-0.91 (0.6)	-0.78 (0.72)	§t (df=23.6) = -0.50; p = 0.62
alpha1 (8 - 10 Hz, log), mean (SD)	-0.47 (0.99)	0.19 (1.16)	§t (df=23.8) = -1.60; p = 0.12
alpha2 (10 - 12 Hz, log), mean (SD)	0.19 (1.05)	-0.09 (0.96)	§t (df=25.9) = -0.73; p = 0.47
beta1 (12 - 15 Hz, log), mean (SD)	-1.33 (0.77)	-0.128 (0.68)	§t (df=26) = -0.19; p = 0.85
beta2 (15 - 25 Hz, log), mean (SD)	-2.01 (0.65)	-1.86 (0.68)	§t (df=25.0) = -0.83; p = 0.41
beta 3 (25 - 30 Hz, log), mean (SD)	-2.73 (0.63)	-2.41 (0.82)	§t (df=22.5) = -1.2; p = 0.25

\*Fisher's exact test for Count Data; †Wilcoxon rank sum test with continuity correction;  
‡Pearson's Chi-squared Test for Count Data; §Student's t-Test. "Log" indicates that variable was transformed by natural logarithm.

**Table 3: Results of linear regression analysis**

qEEG spectral band	Estimate [b]	[CI 95%]	p-value of interaction
<b>Delta (Overall Model)</b>			
Negative symptoms of ARMS-T	b = 0.12	[-0.10, 0.35]	0.016
Negative symptoms of ARMS-NT	b = -0.26	[-0.45, -0.07]	
<b>Theta (Overall Model)</b>			
Negative symptoms of ARMS-T	b = 0.24	[-0.13, 0.60]	0.033
Negative symptoms of ARMS-NT	b = -0.31	[-0.62, 0.00]	
<b>Alpha1 (Overall Model)</b>			
Negative symptoms of ARMS-T	b = 0.13	[-0.54, 0.80]	0.331
Negative symptoms of ARMS-NT	b = -0.32	[-0.90, 0.25]	
<b>Alpha2 (Overall Model)</b>			
Negative symptoms of ARMS-T	b = 0.14	[-0.47, 0.75]	0.323
Negative symptoms of ARMS-NT	b = -0.24	[-0.76, 0.28]	
<b>Beta1 (Overall Model)</b>			
Negative symptoms of ARMS-T	b = 0.20	[-0.20, 0.60]	0.036
Negative symptoms of ARMS-NT	b = -0.39	[-0.73, -0.05]	
<b>Beta2 (Overall Model)</b>			
Negative symptoms of ARMS-T	b = 0.09	[-0.30, 0.48]	0.175
Negative symptoms of ARMS-NT	b = -0.27	[-0.61, 0.06]	
<b>Beta3 (Overall Model)</b>			
Negative symptoms of ARMS-T	b = -0.07	[-0.52, 0.38]	0.933
Negative symptoms of ARMS-NT	b = -0.06	[-0.45, 0.32]	

**Kommentar [p1]:** Liesse sich b= nicht unter Estimate einfügen und so eine Spalte 'sparen'?

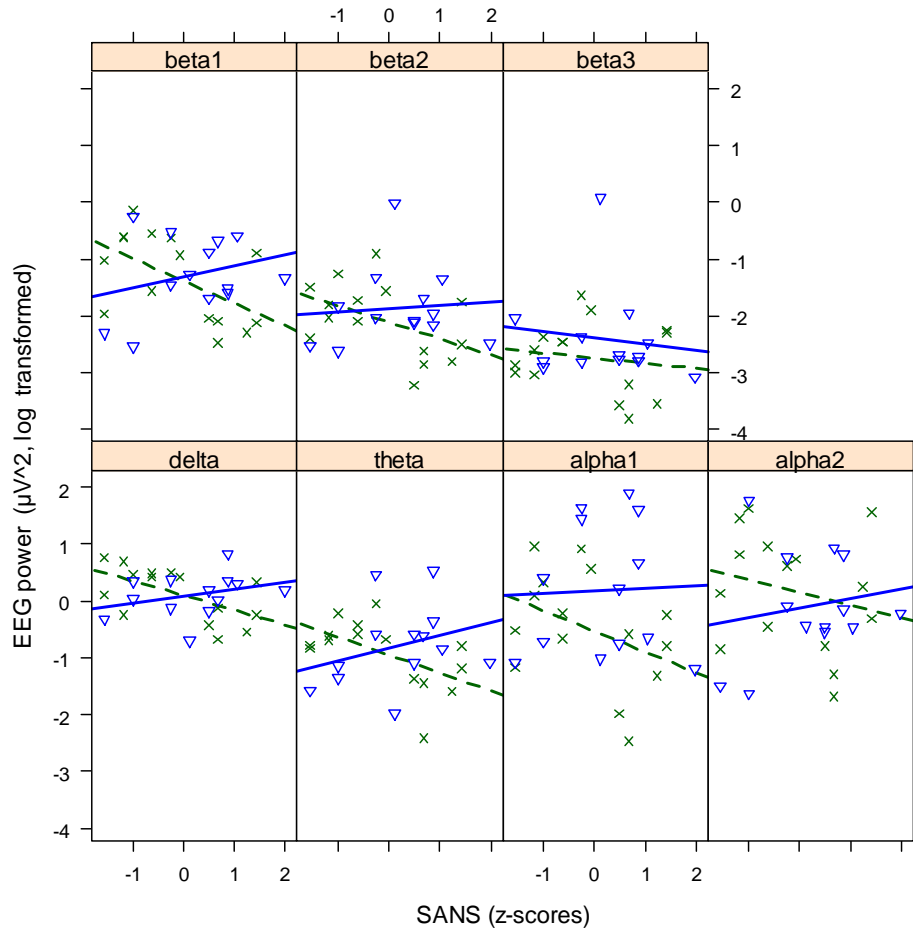
Note: Table 3 shows group specific estimates and confidence intervals of the correlation of EEG power and SANS summary score in seven frequency bands derived from stratified linear models. P-value of interactions of negative symptoms with group indicates if the correlation in the respective band behaves differently according to group (ARMS-T vs. ARMS-NT).

**Table 4: Results of logistic regression analysis**

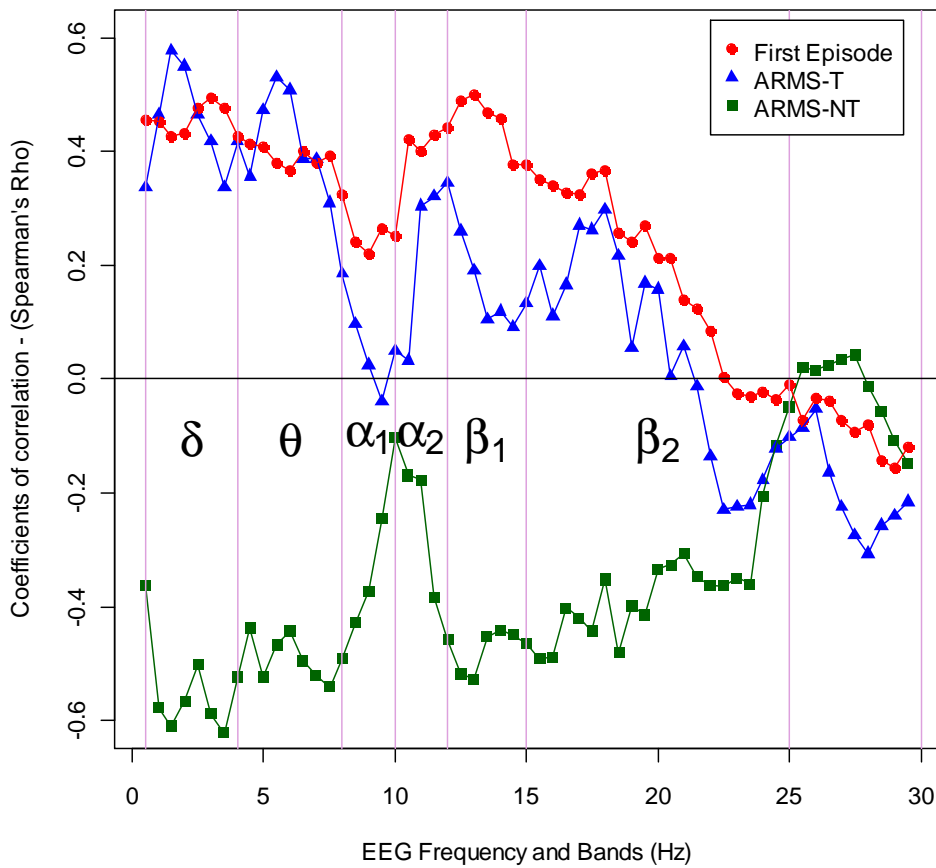
Variables	Estimate	Std. Error	Statistic	p-value	R <sup>2</sup>	Cut-off	PCC	Sens Spec	PPV NPV
<b>Model Delta</b>				0.024					
Delta absolute power	b = -0.51	1.29	z = -0.39	0.694	0.38	0.40	0.82	0.92 0.73	0.75 0.92
Negative symptoms	b = -0.09	0.54	z = -0.17	0.867					
Interaction (Power*Negative Symptoms)	b = 4.08	1.81	z = 2.26	0.024					
<b>Model Theta</b>				0.001					
Theta absolute power	b = 0.31	1.03	z = 0.30	0.761	0.58	0.35	0.89	0.92 0.87	0.86 0.93
Negative symptoms	b = 6.17	2.47	z = 2.50	0.012					
Interaction (Power*Negative Symptoms)	b = 5.96	2.48	z = 2.41	0.016					
<b>Model Alpha1</b>				0.097					
Alpha1 absolute power	b = 0.62	0.46	z = 1.36	0.174	0.27	0.61	0.71	0.46 0.93	0.86 0.67
Negative Symptoms	b = 0.95	0.59	z = 1.61	0.108					
Interaction (Power*Negative Symptoms)	b = 0.90	0.64	z = 1.41	0.158					
<b>Model Alpha2</b>				0.556					
Alpha2 absolute power	b = -0.18	0.43	z = -0.41	0.680	0.01	0.50	0.71	0.69 0.73	0.69 0.73
Negative Symptoms	b = 0.34	0.40	z = 0.84	0.399					
Interaction (Power*Negative Symptoms)	b = 0.38	0.42	z = 0.89	0.372					
<b>Model Beta1</b>				0.041					
Beta1 absolute power	b = 0.79	0.74	z = 1.07	0.283	0.34	0.44	0.82	0.92 0.73	0.75 0.92
Negative Symptoms	b = 3.13	1.34	z = 2.34	0.019					
Interaction (Power*Negative Symptoms)	b = 1.82	0.79	z = 2.32	0.021					
<b>Model Beta2</b>				0.032					
Beta2 absolute power	b = 0.51	0.77	z = 0.66	0.508	0.36	0.43	0.82	0.85 0.80	0.79 0.86
Negative Symptoms	b = 6.81	3.09	z = 0.20	0.028					
Interaction (Power*Negative Symptoms)	b = 2.88	1.33	z = 0.17	0.030					
<b>Model Beta3</b>				0.457					
Beta3 absolute power	b = 0.84	0.71	z = 1.19	0.235	0.12	0.45	0.75	0.77 0.73	0.71 0.79
Negative Symptoms	b = 0.00	2.64	z = 0.00	0.999					
Interaction (Power*Negative Symptoms)	b = -0.15	0.97	z = -0.15	0.879					

Kommentar [p2]: dito

Note: Table 4 shows results of logistic regression models predicting transition to psychosis in ARMS patients based on the combination of negative symptom score and power scores in seven frequency bands. The last columns of the table show Nagelkerke's R<sup>2</sup> index, the optimal cut-off values, percentage of correctly classified individuals (PCC), sensitivity and specificity as well as positive predictive values (PPV) and negative predictive values (NPV) for the logistic regressions.



**Figure 1** Scatterplots of negative symptoms (SANS summary scores, z-transformed) and EEG power in seven frequency bands for ARMS-T ( $\Delta$ ) and ARMS-NT (x) patients



**Figure 2** Correlation coefficients of EEG spectral power at different frequencies with SANS summary scores for ARMS-T and ARMS-NT patients. Greek letters represent the bands as they were defined for the linear regression analysis. Results of first episode (FE) patients<sup>28</sup> are displayed for comparison. 59 % of FE patients were male, mean age was 32 years (9.8 SD), 3 were on antidepressants, 4 on benzodiazepines, 8 used cannabis. Mean SANS summary score in FE patients was 7.4 (4.6 SD).

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