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Association of impaired EEG mu wave suppression, negative symptoms and social functioning in biological motion processing in first episode of psychosis

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Abstract

Background—Event related desynchronization (ERD) of mu waves, or mu suppression, over sensorimotor cortex has been observed in response to self-generated movement, viewing movement, or imaging movement. Mu suppression is especially pronounced when the movement has social relevance and is being generated by a biological entity indicating successful social adaptation. And since social adaptation problems are common in schizophrenia, the authors designed a study to test mu wave suppression in a first episode of psychosis population.

Methods—A total of 32 subjects (first episode of psychosis patients N=20; healthy comparison subjects N=12) aged 13–34 watched movement videos with and without socially relevant cues, executed by biological or non-biological agents. Scalp electrode EEG recordings of mu rhythm (8–13Hz) over sensorimotor cortex during the session were used to calculate mu wave suppression. Average mu suppression was compared within and between groups, as well as correlations between mu suppression and clinical measures.

Results—First episode patients showed significantly reduced mu wave suppression over sensorimotor cortex when viewing biological motion, compared to healthy subjects. In addition, negative symptom burden and poor social adjustment correlated with impaired mu wave suppression.

Conclusions—Our finding provides the first description of impaired event related desynchronization of mu waves in response to biological motion and its correlation with negative symptoms and social adjustment in the first episode of psychosis. Future studies can be conducted to determine if mu wave suppression represents an endophenotype with potential applications in biological treatments of negative symptoms and social functioning deficits in schizophrenia.

Keywords

first-episode psychosis; mu suppression; biological motion; negative symptoms; social adjustment

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1. Introduction

The mu rhythm is an EEG oscillation in the 8–13Hz band, detected over sensorimotor cortex. Large amplitude, synchronous mu waves found at rest, transition to smaller amplitude desynchronous waves when a subject performs a motor activity (Gastaut 1952, Pineda 2005). This phenomenon of event related desynchronization (ERD) or “mu wave suppression” is also observed when a subject watches someone else perform an action (Muthukumaraswamy et al. 2004), or imagines an action being performed (Pfurtscheller et al. 2006). Additional studies suggest that mu oscillations are especially responsive to motor activity in a social context originating from a biological agent rather than an inanimate object (Oberman et al. 2007). Experiments involving typical participants have linked EEG mu suppression to higher order social information processing (Oberman 2007), theory of mind (Perry et al. 2010, Pineda and Hecht 2009), and empathy (Cheng et al. 2008, Cheng et al. 2008), implying a connection between mu suppression and social adaptation. In addition, studies in autism, a disorder with striking social deficits, have demonstrated reduced mu wave suppression in autistic children with otherwise normal intelligence (Martineau et al. 2004, Oberman et al. 2005, Ramachandran and Oberman 2006).

Taken together, these findings suggest that mu wave suppression measures the workings of a neural network integral to the processing of socially adaptive environmental stimuli. It is plausible that aberrant network processing may be present in other psychiatric disorders with social deficits, not just autism, thereby representing a common pathway for impaired social adaptation.

To test this hypothesis, we designed a study assessing mu wave suppression in subjects in a first episode of psychosis (FE) in response to observation of socially relevant movement videos originating from biological agents. Since schizophrenia is a neuro-developmental disorder, studying early stages of psychosis could provide insights into pathogenesis of the disorder, with implications for treatment and prevention.

2. Experimental/ Materials and methods

2.1 Subjects

All subjects, 20 FE and 12 normal controls (NC) provided consent for the study (IRB#090383). This project was reviewed and approved by the UCSD Human Research Protections Program. FE subjects were recruited as part of the Cognitive Assessment and Risk Evaluation (CARE) program based in the UCSD Outpatient Psychiatric services clinic. The program is well known in the San Diego area and receives referrals from community clinics, local schools and private psychiatrists. Control subjects were recruited through advertisements in local newspapers and online sources including Craigslist.

Each subject underwent a clinical assessment using the Structured Clinical Interview for DSMIV (SCID) for Axis I disorders (Pincus et al. 1996). FE subjects' symptoms were scored on the Schedule for Assessment of Negative Symptoms (SANS), Schedule for Assessment of Positive Symptoms (SAPS) (Andreasen 1990) and Social Adjustment Scale – Self report (SAS-SR) (Weissman and Bothwell 1976). The SAS-SR is a 42 item self-administered questionnaire that assesses affective and instrumental performance in occupational role, social and leisure activities, relationship with extended family, marital role, parental role, family unit, and economic independence. The scale provides subscale and overall scores, where a higher score represents greater impairment in functioning. All subjects were rated on the Global Assessment of Function (GAF) scale (Hall 1995, Hall and Parks 1995).

We included anyone who met criteria for a first episode of psychosis within the last 2 years, and excluded those with a history of a traumatic brain injury or seizure disorder. Subjects with a history of substance abuse or dependence in the last month per history or urine toxicology screen were excluded.

Our sample of 32 subjects (20 FE subjects and 12 control subjects) was comparable in terms of gender and handedness. FE subjects were younger on average $t(30)=2.4$, $p<0.05$ and had significantly lower scores on GAF $t(30)=7.5$, $p<0.001$ and SAS-SR $t(30)=-2.7$, $p<0.05$, compared to controls (Table 1). Seventeen of the 20 subjects in the FE group were taking psychotropic medications at the time of testing. All participants had normal or corrected-to-normal vision.

2.2 Mu Suppression Procedure

EEG data were collected while subjects watched videos of specified movement conditions on a 20-inch Dell computer monitor (resolution: 1440 by 900 pixels) at a viewing distance of 96 cm, corresponding to 4.5 degree viewing angle. Videos consisted of movement actions 3–4 seconds long that were looped and presented for 80 seconds. All of the images were $7.5\text{cm} \times 7.5\text{cm}$ in size and centered on the screen. Each video was presented twice in random order. The following conditions were presented (Figure 1):

- (1) Baseline/ Ball condition: Video of two bouncing balls: two light gray balls (32.9 cd/m²) on a black background (1.0 cd/m²) moved vertically towards each other touched in the middle of the screen then moved apart to their initial starting position. This condition of two moving inanimate objects has been used as a baseline condition in previous studies of mu suppression (Oberman 2005).
- (2) Moving hand condition: Subjects viewed a black and white video of an experimenter opening and closing the right hand at approximately once per second. The hand was medium gray (8.6 cd/m²) on a black background (3.5 cd/m²). In autism studies, affected children showed reduced mu suppression when viewing a moving hand compared to age matched controls (Oberman 2005).
- (3) Social interactive condition: In this condition, the subjects watch a game of catch between with three people throwing a ball to each other. Occasionally, the ball is thrown towards the screen as if the subject is a participant in the game being played. The social context of the biological movement in this condition leads to mu suppression compared to non biological movement in typical populations (Oberman 2007).
- (4) Biological motion/ Point light display animation: This video is created by placing 12 lights on major joints of a person's body and filming the person jumping rope in the dark. The sparse visual information provided in these types of displays requires global integration of motion signals (Ahlstrom et al. 1997), and has been shown to suppress mu waves in typical subjects (Ulloa and Pineda 2007).

The movements in each video occurred at a frequency of 1Hz and a continuous performance task was included to ensure that subjects were attentive to the stimulus. For instance, in the ball condition, the balls came to a stop for a 1 second interval, 5 times, for the duration of the condition. Subjects were instructed at the beginning of the task to stay alert and attend to videos, to count and report the number of “stops” in each condition. Subjects were also instructed to minimize body movements.

2.3 EEG data acquisition and analysis

Two disk electrodes were applied behind each ear (mastoids) to serve as linked reference electrodes and one on the forehead to act as ground. Data were collected from 5 electrodes applied directly to the scalp at the following locations: C3, Cz, C4, O1 and O2, using the international 10–20 method of electrode placement. Following head measurement and determination of the electrode location, skin surface was lightly abraded to reduce impedance before applying electrolytic gel and electrodes. The impedances on all electrodes were measured and confirmed to be less than 10 KOhm prior to testing. Once the electrodes were in place, subjects were seated in a quiet room in front of a computer monitor screen.

EEG was recorded and analyzed using Neuroscan Synamps 4.2 system (bandpass 0.1–30 Hz). Data were collected for 80 s per condition at a sampling rate of 500 Hz. Per standard protocols, data from the first and last 10 seconds of each block were removed to eliminate attentional transients due to initiation or termination of the stimulus. A 1-min segment of data following removal of initial and terminal 10 s was obtained and combined with the other trial of the same condition, resulting in one 2-min segment of data per condition. Eye and body movement related EEG segments, and any artifact activity were identified and eliminated prior to analysis.

Data were segmented into epochs of 2 seconds beginning at the start of the segment. Data were only analyzed if there were at least 40 epochs available after rejection of artifacts. For each segment, integrated power in the 8–13 Hz range was computed using a Fast Fourier Transform performed on the epoched data (1024 points). A cosine window was used to control for artifacts resulting from data splicing. Mu suppression was calculated for central (C3, Cz and C4) and occipital (O1 and O2) sites using the equation: $\text{Mu suppression} = \log_{10}(\text{mu power of experimental condition} / \text{mu power of ball condition})$ (Oberman et al. 2008). A log ratio less than zero indicates mu suppression, a log ratio equal to zero indicates lack of mu wave suppression and a log ratio greater than zero indicates mu enhancement.

A ratio was used to control for variability in absolute mu power as a result of individual differences such as scalp thickness and electrode impedance. The ratio to the ball condition was computed in order to control for attention to counting or any effects due to stimulus stopping during the continuous performance task and processing of directional motion (Oberman 2008). Ratio data are inherently non-normal as a result of lower bounding, as such, we used a log transform for analysis.

3. Results

In order to investigate group differences in mu suppression, a repeated measures analysis of variance (ANOVA) with condition (moving human hand, social interaction, biological motion) and electrode site (C3, Cz, C4) as the within-subject variable and diagnostic group (NC, FE) as the between-subject variable was performed. Since age was significantly different between the two groups, age was used as a covariate for comparisons between the two groups.

3.1 Variability between groups

There was a significant main effect of condition $F(2, 58) = 3.9, p < 0.05$ and a significant condition X group interaction effect $F(2, 58) = 5.5, p < 0.01$. There was no significant effect of age or electrode site. Condition X group interactions were decomposed further using electrode site (C3, Cz and C4) as a within subject factor, diagnostic group as a between subjects factor and age as a covariate for each condition using repeated measures ANOVAs. The analysis revealed a significant difference in mu suppression between groups for the biological motion condition $F(1, 29) = 10.4, p < 0.01$, but not for moving hand or social

interaction conditions (Figure 2). Additionally, there were no group differences in mu suppression at the occipital sites, thus eliminating the possibility of posterior alpha influence on mu rhythm recordings.

3.2 Variability within groups

We used repeated measures ANOVA with mean mu suppression across frontocentral sites (C3, Cz and C4) as the within subjects factor across conditions within each diagnostic category (normal controls or first-episode subjects) separately, using a 3×1 design. There was no main effect of condition in NC group. There was a significant main effect of condition in the FE group $F(2, 36) p < 0.01$. Post-hoc analysis revealed significant differences between condition 2 and 4 (moving hand and biological motion, $F(1, 19) = 11.3$, $p < 0.01$) and condition 3 and 4 (social interaction and biological motion, $F(1, 19) = 15.7$, $p < 0.01$), but not between condition 2 and 3 (moving hand and social interaction), with suppression being lowest for biological motion, and highest for the social interaction condition.

3.3 Correlational analyses

Relationships between mu suppression for the biological motion condition at frontocentral sites and SANS, SAPS, GAF and SAS-SR ratings were investigated in exploratory analyses using Spearman rank correlations in first episode subjects.

A statistically significant correlation was noted between total negative symptoms and mu wave suppression in response to viewing biological motion at C3 (Spearman's $\rho = 0.50$ $p < 0.05$) and Cz (Spearman's $\rho = 0.67$ $p < 0.01$) (Figure 2), such that subjects with the highest negative symptom ratings showed lowest mu wave suppression. Further exploration of the individual SANS items showed significant correlations with the anhedonia subscale across all three frontocentral electrodes (C3: Spearman's $\rho = 0.46$, $p < 0.05$; Cz: Spearman's $\rho = 0.65$, $p < 0.01$; C4: Spearman's $\rho = 0.46$, $p < 0.05$).

No statistically significant correlations were found between mu suppression and total SAPS, or GAF.

There was a statistically significant correlation between overall social functioning and mu suppression at Cz (Spearman's $\rho = 0.50$ $p < 0.05$). Further exploration within the subscales showed statistically significant correlations between the social subscale of the SAS-SR and mu suppression at two out of three frontocentral electrode sites (Cz: Spearman's $\rho = 0.47$ $p < 0.05$; C4: Spearman's $\rho = 0.59$ $p < 0.01$) (Figure 3). On the SAS-SR scale, higher scores imply poor social functioning, which was correlated with reduced mu wave suppression.

4. Discussion

This is the first study of event related desynchronization (ERD) of mu rhythm over sensorimotor cortex in individuals experiencing a first episode of psychosis. Compared to typically developing individuals, first episode subjects showed similar mu wave suppression when viewing 1) a moving human hand and 2) a social interaction depicted by a game of catch. FE subjects showed significantly lower mu wave suppression when viewing biological motion in a point light display animation video.

Point light animation videos are created by filming a person in the dark with lights on major body joints, while performing a repetitive motion such as walking or jumping. These displays provide sparse visual input that requires “filling-in” to recover object information to identify the kind of motion being produced (e.g., walking, jumping, dancing), and the identity of the agent (Blake and Shiffrar 2007). Neural processing of biological motion is an

evolutionarily conserved mechanism that plays a fundamental role in social adaptation (Klin et al. 2007, Simion et al. 2008). For instance, both newly hatched chicks (Vallortigara et al. 2005) and 2-day old human infants preferentially attend to biological motion in point-light displays (Simion 2008), compared to random motion. It has been suggested that attention to biological motion facilitates filial attachment forming the basis for subsequent social development (Johnson 2006). Reduced mu wave suppression to point light animations, but not other types of biological movement in first episode patients has important implications. It is conceivable that the impoverished stimuli in point light displays place higher integration demands than rich visual input from full images of individuals performing actions, and thus uncover deficits that are otherwise compensated in early psychosis.

Within subject analysis conducted for each group showed that mu wave suppression did not vary between the three conditions in the control group. For the FE group, statistically significant difference in mu wave suppression between conditions was driven by impaired suppression to biological motion, but not the other two conditions, again, highlighting a specific impairment in processing abstract, impoverished stimuli rather than a global deficit.

Additionally, beyond group differences, there was a relationship between mu wave suppression and 1) negative symptoms and 2) social adjustment, such that impaired mu wave suppression was correlated with increased negative symptoms and poor social adaptation. In general, negative symptoms emerge early in the disease process, are linked with reduced social functioning and poor functional outcomes in schizophrenia (Blanchard et al. 2005, Dominguez et al. 2010, Ho et al. 1998, Milev et al. 2005). It is felt that the SANS, frequently used to measure negative symptoms, in fact contains items that reflect social functioning (Horan et al. 2006, Horan et al. 2006). Interestingly, the anhedonia subscale relies solely on patients' report of capacity to not only experience pleasure, but to engage in recreational and social activities. Therefore, it is plausible that the correlations with the anhedonia subscale of SANS and social and leisure subscale of SAS-SR, essentially reflect a relationship between mu suppression and social interactions. Thus, the correlation between mu wave suppression, which is known to be modulated by social inputs, and social functioning, provides evidence for construct validity.

The study is limited in scope by several factors. First, the small sample size and significant difference in age between groups, limits the generalizability of these results. Many of the first episode subjects in our study were taking antipsychotic medications at the time of testing, a factor whose impact on mu suppression cannot be parsed out without a larger sample size. The second limitation results from constraints inherent to conventional EEG paradigms, which cannot provide information regarding the source of the electrical activity, nor relationships between distinct brain regions during response to a stimulus. Nonetheless, the study provides a first description of quantitative differences in neural processing of biological motion in first episode psychosis by measuring mu wave suppression over sensorimotor cortex. Perhaps, more importantly, the study links negative symptoms and social functioning to a quantifiable electrical oscillation that can be measured easily through scalp EEG recordings. Further studies can be conducted to determine if mu wave suppression represents an endophenotype with potential applications in biological treatments of negative symptoms and social functioning deficits in schizophrenia.

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Figure 1.

Baseline and Experimental conditions^a

^aAdapted from Obeman et al 2008, Condition 1: Baseline: Moving balls, Condition 2: Moving human hand, Condition 3: Social Interaction, Condition 4: Biological motion.

Figure 2.

Comparison of average mu wave suppression over frontocentral sites by condition in first episode psychosis patients versus normal controls

^aMu suppression = $\log_{10} (\mu \text{ power experimental condition} / \mu \text{ power ball condition})$, ^b $p < 0.01$, Condition 2: Moving human hand, Condition 3: Social Interaction, Condition 4: Biological motion.

Figure 3.
Relationship between mu wave suppression and social adjustment in first episode of psychosis patients

^aSAS-SR = Social Adjustment Scale – Self Report, Spearman's rho=0.50 p<0.05

Table 1

Subject characteristics

Variable	Normal Control (NC)	First episode (FE)
N	12	20
Mean Age in years (SD)	23.75 $\pm$ 5.8 ^a	19.15 $\pm$ 4.3
Age Range in years	14–34	14–33
Gender (% Male)	50%	80%
Handedness (% Right handed)	95%	92%
Global Assessment of function (GAF)	82 $\pm$ 18 ^b	46 $\pm$ 11
Social Adjustment Scale - Self report (SAS-SR)	2.4 $\pm$ 0.6 ^a	1.8 $\pm$ 0.5
Schedule for Assessment of positive symptoms (SAPS)	N/A	5.1 $\pm$ 5.4
Schedule for Assessment of negative symptoms (SANS)	N/A	9.9 $\pm$ 6.4

^a p<0.05^b p<0.001