Disordered visual processing and oscillatory brain activity in autism and Williams Syndrome

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Two developmental disorders, autism and Williams syndrome, are both commonly described as having difficulties in integrating perceptual features, i.e. binding spatially separate elements into a whole. It is already known that healthy adults and infants display electroencephalographic (EEG) γ-band bursts (around 40 Hz) when the brain is required to achieve such binding. Here we explore γ-band EEG in autism and Williams Syndrome and demonstrate differential abnormalities in the two phenotypes. We show that despite putative processing similarities at the cognitive level, binding in Williams syndrome and autism can be dissociated at the neurophysiological level by different abnormalities in underlying brain oscillatory activity. Our study is the first to identify that binding-related γ EEG can be disordered in humans. *NeuroReport* 12:2697–2700 © 2001 Lippincott Williams & Wilkins.

Key words: Autism; Binding; EEG; ERP; Face processing; γ; Visual perception; Williams Syndrome

INTRODUCTION

Williams Syndrome (WS) and autism are both developmental disorders in which visual processing of static objects is dominated by local features as opposed to global or configural properties of an array [1,2]. This apparent failure to integrate components into whole units is manifest in many cognitive domains in both syndromes [3,4], and is sometimes referred to as weak central coherence [1]. Faces are important stimuli for which this abnormal dominance of local feature over global configural cues is particularly evident. In normal adults the perception of the human face relies on configural information; an upright face is perceived with the global configuration taking precedence over the individual parts [5]. Inverting the face, however, disrupts configural processing, and accuracy at identifying the face is significantly reduced [6]. People with WS or autism are unusual in that they display a reduced inversion effect and appear to rely less than controls on configuration [2,7,8]. The similar result for these two disorders is striking because in most other ways they have dissimilar behavioural profiles.

The neural basis of the visual processing abnormalities in autism and WS is, as yet, unclear but the apparent failure to integrate features together to compose whole objects may be related to binding processes in the brain. Recent evidence from both cellular recording and scalp-recorded EEG has linked γ band neural oscillations to the binding process [9–11]. For example, a burst of γ band EEG is induced around 250 ms after presentation of an illusory object such as a Kanizsa figure [10,12], or an upright Mooney face [13]. However the most stringent test of the relationship between binding and γ band activity has not been applied. γ band EEG has never been studied in humans with difficulties in perceptual binding; if the processes underlying γ band EEG are necessary for achieving binding then they should be different, and reflected in the EEG during binding tasks, in these populations.

To test our hypotheses that binding related γ band EEG in the two disorders would be both different to normal, we presented pictures of upright and inverted human faces to three groups of participants: a normal adult control group, a group with WS and a group with autism. While passively viewing the faces, EEG was recorded from each participant by means of a Geodesic sensor net composed of 128 electrodes. The recording was then subjected to a time-frequency analysis to give a measure of induced γ band activity.

MATERIALS AND METHODS

Participants: Participants were eight individuals with WS (confirmed by clinical and genetic analyses), eight individuals with autism spectrum disorder (confirmed by clinical

analysis) and eight normal adult controls. Groups were matched on chronological age and handedness. Mean ages were 30.9, 36.3 and 30.9 years, respectively.

Stimuli: Stimuli consisted of 97 colour pictures of adult female faces presented at 12.1° visual angle a total of 194 times with 50% of the stimuli in the inverted position.

Procedure: Experiments took place in a dimly lit, sound proofed, and electrically shielded booth. The electroencephalogram (EEG) was recorded using a Geodesic Sensor Net of 128 electrodes, against a vertex reference, amplified with 0.1–100 Hz bandpass filtering. The recording was digitized at a 250 Hz sampling rate, stored on a computer disk and segmented offline into EEG trials with 200 ms pre-stimulus and 900 ms post-stimulus onset duration.

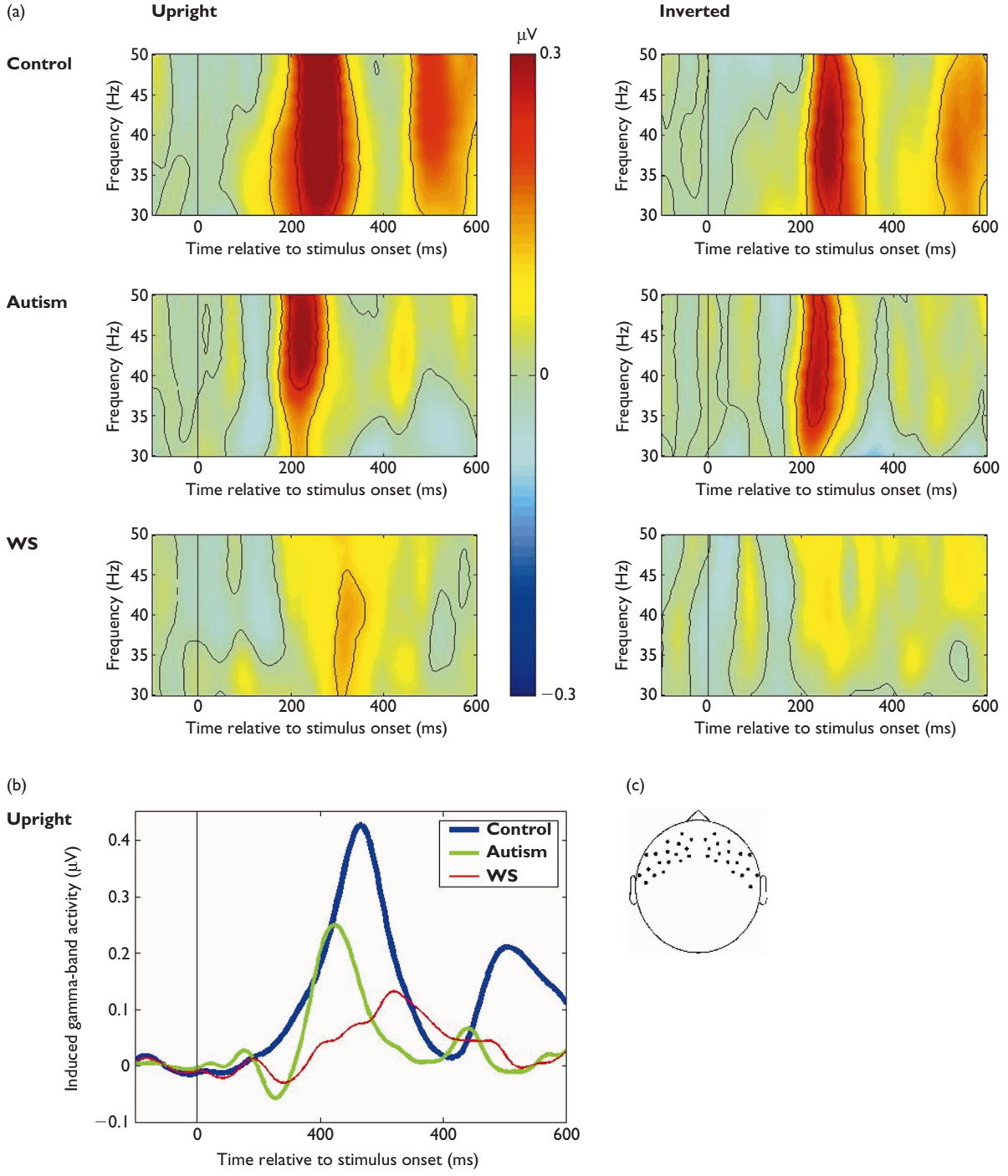

Fig. 1. (**a**) Time–frequency plots showing induced γ-band activity by orientation for each group. (**b**) Graph shows averaged γ-band activity over time for each group in the upright face condition. (**c**) Top down view of the head with electrode locations used for analysis marked as black filled circles.

Movement and electrical artefacts were identified and rejected by trial-by-trial inspection of the recorded EEG. Individuals with <24 valid artefact-free trials in either condition were excluded.

Wavelet analyses: A time–frequency analysis of the data was performed using a continuous wavelet transform. The Morlet wavelet was employed. This is a complex function of time, t, defined as:

$$w(t, f) = \frac{1}{\sigma_t\sqrt{\pi}} \exp\left(\frac{-t^2}{2\sigma_t^2}\right)\exp(2i\pi ft)$$

A set of wavelets with frequencies, f, covering the 21–60 Hz range at intervals of 1Hz were used, and the parameter σ_t was defined as $\sigma_t = 3.5/\pi f$.

To calculate induced activity the transform was applied to all EEG signals recorded at each channel across all individual trials. For evoked activity the transform was applied to the EEG signal after averaging across trials. The coefficients, E(t,f), of the wavelet transform at a particular frequency, f, were calculated by convolving the EEG signal, s(t), with the wavelet, w(t,f), and taking the modulus of the resulting complex coefficients:

$$E(t, f) = |s(t) \times w(t, f)|.$$

E(t,f) represents the time-varying amplitude of the signal within a frequency band centered on f. The mean value of E(t,f) during the 100 ms prior to stimulus onset was considered to be the baseline level and was subtracted from E(t,f). Average coefficients, for each subject, were calculated by taking the mean across trials, and grand average coefficients were calculated by taking the mean of the subject averages. In each case, E(t,f) was also averaged across frequencies in the range 32–48 Hz to provide a single, time-varying, measure of the γ-band activity. Channel groups were selected in frontal scalp regions on the basis of previous studies. Electrode sites are illustrated in Fig. 1c.

ERP analyses: The ERPs were digitally filtered with an elliptical low-pass filter at 30 Hz and converted to an average reference. Channel groups were selected in the bilateral temporal-occipital areas illustrated in Fig. 2c. Paired sample *t*-tests (one-tailed), comparing upright and inverted peak data (amplitude or latency) were carried out for each group.

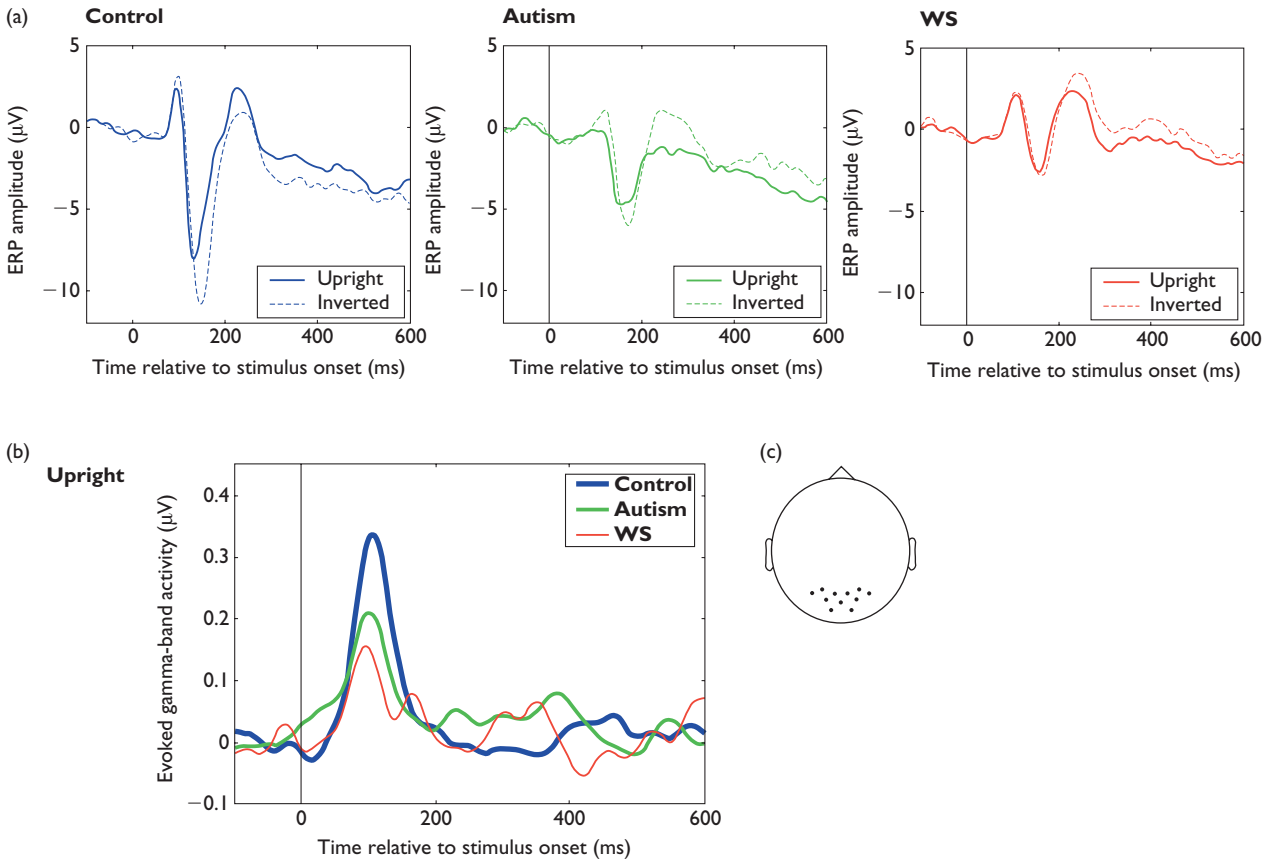

Fig. 2. N170 component ERPs. Electrode = T5 (10-20 system). Control group illustrate typical effect of bigger amplitude ($t(7) = 7.85$, $p < 0.05$) and longer latency ($t(7) = 5.30$, $p < 0.05$) to inverted than to upright faces. Autism group show only an effect in amplitude ($t(7) = 2.19$, $p < 0.05$) and WS group only an effect in latency ($t(7) = 2.82$, $p < 0.05$). That there is some effect of inversion indicates that the brain is at least detecting changes in face orientation. (**b**) The early phase locked γ burst over occipital scalp locations. (**c**) Occipital electrode sites used for ERP and phase locked γ burst analysis are marked as black filled circles.

RESULTS

Results for our control group were very comparable to those reported by Rodriguez and colleagues [13]. The γ burst to pictures of real faces (see Fig. 1a) was located over frontal scalp regions and was consistent with previous results, i.e. larger in the upright compared to the inverted condition (Wilcoxon $T = 2$, $Z = -2.24$, $p < 0.05$). In contrast, γ in the WS and autism groups was unaltered by condition (Fig. 1a). This is despite event-related potential (ERP) evidence of activity below 30 Hz (Fig. 2a), indicating that face orientation was detected by the brain in all groups. While face orientation did not modulate the size of the γ activity in either the Williams Syndrome or the autism group, the nature of the γ burst was qualitatively different for each group. Figure 1b illustrates that averaged activity in the WS group was not organised into a clear burst in the same way as the other two groups; rather it was smeared across a longer time period. Inspection of individual plots showed no evidence of any large amplitude bursts comparable to those seen in the control participants. Despite this, peak latency was not significantly different to the other groups, and the amplitude over the whole period of 200–500 ms was clearly different from baseline (Wilcoxon $T = 4$, $Z = -1.96$, $p < 0.05$). There were no differences in baseline activity between groups. The difference in γ band activity between groups was not reflected in early occipital phase-locked activity, analysis of which showed no significant differences (Fig. 2b). Our results indicate that there are abnormalities in binding-related γ oscillations in both autism and WS. However, the nature of these effects is different in the two cases. In autism, apparently normal bursts of γ activity occurred, but the bursts were not different for the upright and inverted faces. In WS, no clear γ bursting occurred, with γ activity being smeared across longer time intervals.

DISCUSSION

Aberrant γ burst patterns may cause a range of binding-related deficits in one or both of these disorders. Alternatively, atypical γ-band activity may also be symptomatic of a more primary deficit. In the case of autism, γ bursting looks very similar to that in controls apart from not being normally modulated by the orientation of the stimulus. This suggests that the differences in binding may be a consequence of another deficit elsewhere in neural processing and/or reflect a difference in strategy or experience with face stimuli. In the case of WS, γ-band EEG did not occur in the regular task-related way observed in the other groups, but resembled the disorganised pattern seen in very young infants before regular bursting emerges between 6 and 8 months [14]. This raises the possibility that for WS deficits in either neuroanatomical or neurochemical substrates essential for task-related γ bursting disrupt the basic neural processes of binding. Brain anatomy has already been shown to be atypical in both syndromes [15,16], together with evidence of atypical brain chemistry in WS [17]. It is plausible that such gross disruption of γ bursting may have multiple cognitive and behavioural consequences.

CONCLUSION

This study provides convergent evidence for the view that bursting of the γ band EEG is related to binding. In addition it shows that the behavioural similarities between WS and autism can be dissociated at the neurophysiological level. The aberrant patterns of γ-band activity observed in these two developmental disorders may turn out to be primary or secondary causes of the phenotypic outcomes in perception and in other domains. Importantly, the present evidence opens a new channel of investigation in the search for core deficits in different developmental disorders.

We have also analysed our gamma-band for stimulus-related differences in coherence across frontal leads. We find similar results to those presented in this paper for gamma power. There is significantly greater coherence for the upright compared with inverted face condition in the control group only, and bursts of coherence coincide in time and frequency with those reported for gamma power. The groups with autism and Williams Syndrome showed no stimulus-dependent differences in coherence across conditions.

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