Archival Report

Biological Psychiatry: CNNI

Sensory Prediction Errors Are Less Modulated by Global Context in Autism Spectrum Disorder

Judith Goris, Senne Braem, Annabel D. Nijhof, Davide Rigoni, Eliane Deschrijver, Sander Van de Cruys, Jan R. Wiersema, and Marcel Brass

ABSTRACT

BACKGROUND: Recent predictive coding accounts of autism spectrum disorder (ASD) suggest that a key deficit in ASD concerns the inflexibility in modulating local prediction errors as a function of global top-down expectations. As a direct test of this central hypothesis, we used electroencephalography to investigate whether local prediction error processing was less modulated by global context (i.e., global stimulus frequency) in ASD.

METHODS: A group of 18 adults with ASD was compared with a group of 24 typically developed adults on a well-validated hierarchical auditory oddball task in which participants listened to short sequences of either five identical sounds (local standard) or four identical sounds and a fifth deviant sound (local deviant). The latter condition is known to generate the mismatch negativity (MMN) component, believed to reflect early sensory prediction error processing. Crucially, previous studies have shown that in blocks with a higher frequency of local deviant sequences, top-down expectations seem to attenuate the MMN. We predicted that this modulation by global context would be less pronounced in the ASD group.

RESULTS: Both groups showed an MMN that was modulated by global context. However, this effect was smaller in the ASD group as compared with the typically developed group. In contrast, the P3b, as an electroencephalographic marker of conscious expectation processes, did not differ across groups.

CONCLUSIONS: Our results demonstrate that people with ASD are less flexible in modulating their local predictions (reflected in MMN), thereby confirming the central hypothesis of contemporary predictive coding accounts of ASD.

Keywords: ASD, Autism, EEG, Mismatch negativity (MMN), Prediction error, Predictive coding

https://doi.org/10.1016/j.bpsc.2018.02.003

Autism spectrum disorder (ASD) is characterized by severe difficulties in social interaction and communication as well as nonsocial symptoms such as repetitive patterns of behavior and hyper- or hyposensitivities to sensory stimuli (1). Ever since autism was first described, researchers have tried to identify a single cognitive deficit that can account for this heterogeneous set of symptoms. However, most theories have provided an explanation for either the social or sensory symptoms but failed to explain both. A recent evolution in ASD research attempts to fill this gap by using predictive coding to explain both social and sensory symptoms in ASD [(2–5); for a review, see (6)]. Central to many of these accounts [e.g., (2,4)] is the hypothesis that people with ASD show an inflexible precision in regulating their low-level sensory expectations. Here, we put this hypothesis to the test.

The predictive coding framework states that the brain constantly makes predictions about the world and processes incoming sensory information in light of those predictions (7,8). When incoming information is different than expected, the brain generates what is referred to as a prediction error (i.e., a surprise), and this signal can then be used to adapt future predictions. However, an adaptive use of prediction errors to guide behavior requires distinguishing between behaviorally relevant and irrelevant prediction errors based on contextual information. Sometimes prediction errors signify that there are learnable regularities in the environment and predictions should be adapted, while in other contexts prediction errors are just noise in the environment that can be ignored. For example, the unexpected noise of someone clearing her throat could mean something important when in a company meeting (i.e., a social signal) but is more likely to be irrelevant to us when sitting in the doctor's waiting room. Central to our everyday behavior is our ability to dissociate these more informative prediction errors from less informative ones. The mechanism through which this relative weight of bottom-up prediction errors and top-down predictions can be adjusted is often referred to as precision (7). Importantly, it has been proposed that the weighting of prediction error signals is less flexibly adjusted across contexts in ASD (2,4). In other words, ASD is hypothesized to be characterized by an inflexible precision of prediction errors. This hypothesized deficit naturally explains key symptoms of ASD such as difficulties in cognitive flexibility, altered perceptual processing, repetitive behavior, and resistance to change. In fact, according to these authors, a broad range of ASD symptoms can be understood in light of

ISSN: 2451-9022

this deficit, including both sensory and social problems [see (2,4)]. There are differences in the specific hypotheses of these different theories. For example, Van de Cruys and colleagues (4,5,9) emphasized not only inflexible but also consistently high precision of prediction errors. Lawson and colleagues (2,10) similarly hypothesized that there is an inflexible precision of prediction errors due to a failure of attenuating sensory precision. However, while different proposals [e.g., (3,11); for a review, see (6)] have different accents, all of them are based on the idea that there is an inflexible precision of predictions and prediction errors in ASD.

Recent studies already provided preliminary support for the assumption that in individuals with ASD there is an inflexible weighing of the relative importance of sensory prediction errors [e.g., (12–18)]. However, these studies focused mostly on higher-level mechanisms by testing the effects of social manipulations [e.g., (12,17)], expectancy instructions (13), or volatility manipulations in decision making (14). Some behavioral studies focused on more low-level processes by studying movement adaptation (15) or Gabor orientation discrimination (18), but no study has investigated this hypothesis focusing on early sensory processing, which we believe requires the use of neural measurements rather than behavioral paradigms. Therefore, we used a well-validated hierarchical predictive coding task as first introduced by Bekinschtein *et al.* [(19); see also (20,21)] to dissociate the relative weighting of sensory prediction errors in an ASD group and a matched typically developed (TD) control group. The paradigm is an auditory oddball task where participants are presented with sequences of five tones, which consist of either local standards (five identical tones) or local deviants (four identical tones followed by a deviant tone). To determine whether the processing of local deviants can be modulated by global context, the relative frequency of local deviants versus local standards is manipulated across blocks, thereby creating different levels of global expectancy; in some blocks local deviants are rare, while in other blocks they occur frequently. Following the reasoning that less frequent events are often more relevant to us (i.e., they do not match with our global predictions), this context manipulation should induce a larger surprise reaction in blocks where the surprising event is more rare.

Indeed, using this manipulation, a well-replicated finding in TD adults is that event-related potential components of local prediction error processing can be modulated by this global context. To show this, Bekinschtein *et al.* (19) and others dissociated two event-related potential components. First, the onset of the fifth tone in local deviant sequences elicits a very early component called the mismatch negativity (MMN) (22), believed to reflect early sensory prediction error processing in a preattentive and nonconscious manner (21,23,24). Because the MMN is also elicited by unexpected tone omissions, it is thought to represent predictive activity rather than just adaptation to repeated stimuli (21). Second, a later positive deflection with a parietal distribution, the P3b, is elicited, and this reflects top-down attention directed toward a stimulus (25). Consistent with this dissociation, Bekinschtein *et al.* (19) demonstrated that the P3b is sensitive to global expectancies, while the MMN is sensitive to local deviances. However, as shown by Wacongne *et al.* (21), the MMN is also influenced by the global context, showing a smaller amplitude when local deviances are more frequent. This effect shows that processing of local prediction errors is modulated by global context in TD individuals. If individuals with ASD indeed show an impeded ability to modify their local predictions, we expect to see that the amplitude of the MMN should be less modulated by global context in the ASD group compared with the TD group. For the P3b following global deviances, we did not have specific hypotheses.

METHODS AND MATERIALS

Participants

In total, 25 adults with ASD (17 men) and 30 TD adults (22 men) participated in the study. All participants were right-handed and free of hearing problems. Participants in the TD group were screened to have no reported history of neurological or psychiatric disorders. Because the focus was on high-functioning ASD, all participants had a full-scale IQ above 80. A score above the cutoff on either the Autism Spectrum Quotient (32 or higher) (26) or the Social Responsiveness Scale–Adult version (T-score of 61 or higher) (27) was used as an exclusion criterion in the TD group (see also Figure 1). These are the cutoffs as described in the original questionnaires and are meant to screen for autistic traits in an adult population. Therefore, 6 participants were excluded, resulting in 24 remaining TD adults. All participants gave written informed consent before participation and were financially compensated. The study was approved by the local Ghent University ethics committee.

All adults with ASD had received a clinical diagnosis of ASD (n = 19), autistic disorder (n = 2), or Asperger's syndrome (n = 4), prior to the experiment, by an independent clinician or multidisciplinary team. For 1 subject, the clinical diagnosis of ASD was withdrawn by an independent clinician during the study; therefore, this participant was excluded, leaving a total of 24 participants in the ASD group. Within this group, the diagnosis was verified with the Autism Diagnostic Observational Schedule (ADOS) (28) Module 4 by a trained researcher using the revised scoring algorithm (29). In line with earlier ASD studies (30–33), we included only participants with ASD who scored 1 point below the cutoff for ADOS total score or higher (see also Figure 1). As a result, 6 participants were removed from the ASD group. Thus, final data analysis was carried out on 18 subjects in the ASD group (13 men) and 24 subjects in the TD group (16 men). There was no significant difference in age between the two groups, $t_{39.88} = 1.02$, $p = .31$.

Importantly, the results did not change in a statistically significant way when we used the ADOS total score cutoff as the exclusion criterion, resulting in 17 participants in the ASD group. Similarly, our main finding reached the same level of significance when keeping all 24 adults with ASD in the analysis (see Results).

Intelligence was assessed by using the Kaufman 2 short form Wechsler Adult Intelligence Scale–third edition (WAIS-III) as a reliable measure of IQ in ASD (34). For 3 participants with ASD, we used a full WAIS-III that was available and completed within the past 5 years. There was no significant difference in IQ between the two groups, $t_{31.14} = -0.83$, $p = .41$.

Task and Stimuli

We used the paradigm by Bekinschtein *et al.* (19) that dissociates two types of local deviants: local deviants that appear