Abstract

There is a great need for objective measures of perception and cognition that are reliable at the level of the individual subject. Although traditional electroencephalography (EEG) techniques can act as valid biomarkers of cognition, they typically involve long recording times and the computation of group averages. To overcome these well-known limitations of EEG, vision scientists have recently introduced a steady state method known as fast periodic visual stimulation (FPVS). This method allows them to study visual discrimination at the individual level. Inspired by their work, we examined whether FPVS could be used equally effectively to capture abstract conceptual processes. Twenty subjects (20.9 (±2.1) yrs, 6 male) were asked to complete a FPVS-oddball paradigm that assessed their spontaneous ability to differentiate between rapidly presented images on the basis of semantic, rather than perceptual, properties. At the group level, this approach returned a reliable oddball detection response after only 50s of stimulus presentation time. Moreover, a stable oddball response was found for each participating individual within 100s. As such, the FPVS-oddball paradigm returned an objective, non-verbal marker of semantic categorisation in single subjects in under two minutes. This finding establishes the FPVS-oddball paradigm as a powerful new tool in cognitive neuroscience.

1 Introduction

Physicians and psychologists have a long history of measuring people's ability to notice variation. Their interest in doing so frequently arises from the fact that deficits in this ability can signal severe neural impairments. To diagnose colour blindness, for example, physicians typically ask patients to distinguish red from green figures (e.g., using the Ishihara Plate Test, Birch, 1997). Similarly, to detect face blindness, psychologists often require their clients to recognize faces of different individuals (e.g., via the Cambridge Face Memory Test, Bowles et al., 2009). In both cases (as in many other behavioural tests), however, assessing people's ability to distinguish between certain entities requires that they provide active and truthful replies. Yet, some individuals may simply not be able (e.g., children, stroke patients) or willing (e.g., eye witness) to give such replies. Hence, physicians and psychologists are frequently interested in developing tests that can be reliably administered without requiring test-takers' overt replies.

These alternative measures include standard brain imaging techniques, such as electroencephalography (EEG; Chennu et al., 2013) and functional magnetic resonance imaging (fMRI; cf Monti et al., 2010). One popular EEG marker of people's ability to detect variation is known as Mismatch Negativity (MMN). This marker is typically derived by subtracting a person's neural response to a frequently presented standard stimulus from that of a rare oddball stimulus in a so-called oddball paradigm, and can be elicited both with and without the subject's explicit attention (Czigler, 2014; Kimura, 2012; Näätänen, Gaillard, & Mäntysalo, 1978; Näätänen & Michie, 1979). In recent years, there has been growing interest in using the MMN as an early marker of attentional deficits in the pre-symptomatic stages of clinical disorders, such as schizophrenia (see Näätänen et al., 2011 for a review). Meta-analyses have repeatedly demonstrated clear MMN deficits in schizophrenia (Bodatsch, Brockhaus-Dumke, Klosterkötter, & Ruhrmann, 2015; Erickson, Ruffle, & Gold, 2016; Umbricht & Krljes, 2005) however despite decades of converging findings, viable clinical tools for assessing these deficits in a reliable manner are still lacking. The great challenge in the translation of experimental EEG findings into viable clinical tools lies in finding measures that are reliable not only at the group level, but at the level of the individual.

This is not just a challenge with MMN, but with EEG measures more broadly (Duncan et al., 2009). To obtain sufficient Signal to Noise Ratio (SNR) using traditional Event Related Potential (ERP) techniques, for example, subjects must typically complete hundreds or thousands of experimental trials, resulting in long recording times. This problem is compounded in oddball paradigms in which a minimum number of standard stimuli are required between oddball stimuli in order to ensure their "rareness". An alternative to ERPs is the Steady State Visual Evoked Potential (SSVEP), in which periodic visual stimulation elicits a periodic neural response at an equivalent frequency (see Norcia, Appelbaum, Ales, Cottereau, & Rossion, 2015 for a review). Recently a new technique combining oddball paradigms with SSVEPs has shown considerable potential for solving the issues of SNR that have hampered traditional ERP approaches.

To date the approach has been used most commonly in studies of face processing and recognition (Dzhelyova & Rossion, 2014; Liu-Shuang, Norcia, & Rossion, 2014; Liu-Shuang et al., 2016; Rossion, 2014; Rossion et al., 2015). But it has also proven successful in probing low-level visual processing (e.g., orientation encoding; Heinrich et al., 2009a) and basic lexical representations (e.g., word/non-word discrimination; Lochy, Van Belle, & Rossion, 2015). To further advance our understanding of the method's potential, our objective was to extend this approach to other domains of mental processing, specifically to

an example of higher level cognition, such as abstract semantic categorisation. Semantic categorisation refers to people's ability to group information in a manner that highlights conceptual commonalities or differences between different entities (Rosch, 1975). As it can occur at different levels of specificity, the same entities can be classified in many different ways (Mervis & Rosch, 1981).

Common objects such as furniture, for instance, can be categorised into so-called subordinate categories (e.g., as chairs, tables, beds etc., Mack, Gauthier, Sadr, & Palmeri, 2008) which, in turn, can prompt even more fine-grained subordinate classifications (e.g., chairs may be considered dining chairs or office chairs; Tversky & Hemenway, 1984). At the same time, however, furniture can also be categorised according to so-called superordinate categories (e.g., just like vehicles, but unlike tools, as non-graspable objects; Rice, Valyear, Goodale, Milner, & Culham, 2007) which, in turn, can prompt even coarser superordinate classifications (e.g., furniture, vehicles and tools together can count as man-made rather than natural entities; (Caramazza & Shelton, 1998; Rogers & Patterson, 2007). In short, based on a perceiver's domain-specific knowledge (Tanaka & Taylor, 1991) and/or momentary processing goal (Barsalou, 1991),multi-level conceptual hierarchies can provide numerous levels of specificity according to which objects can be categorised.

To gain an even better hold on the mechanisms of semantic categorisation in the human brain, it seems warranted to develop tasks that can objectively quantify an individual's ability to categorise objects upon perception along various levels of semantic specificity. Such a task would not only be of particular experimental value, but could ultimately also inform the assessment of neural disorders characterized by difficulties with semantic categorisation, such as fronto-temporal dementia. We believe that the newly developed FPVS-oddball paradigm lends itself well for such a purpose. The paradigm has already been used to assess the integrity of face processing in prosopagnosia (Liu-Shuang et al., 2016). Inspired by this prospect, the aim of this study was to develop a new version of the FPVS-oddball paradigm to semantic processing. We predicted that increases in power at the oddball stimulation frequencies would be observed when standard and oddball stimuli differed in their semantic categories. We also predicted that

when stimuli were scrambled, therefore removing any semantic category level information, oddball	
responses would not be observed.	

2 Method

2.1 Participants

Twenty adults (aged 18-28, mean age 20.9 (±2.1), 6 males) gave consent to participate in the study. They were recruited from the University of Bristol student population and declared themselves to be in normal health and had normal or corrected-to-normal vision. Ethical approval for our procedures were obtained from the University of Bristol Science Faculty ethics board. Participants provided written informed consent before participating and were free to withdraw from the study at any time.

2.2 Stimuli

Images were selected from a previously validated set of 360 high quality colour images belonging to 23 semantic categories (Moreno-Martínez & Montoro, 2012). Images were selected to form three separate sets expected to prompt semantic categorisation at different levels of specificity. Based on prior work on semantic categorisation (e.g. Chan et al., 2011; Moss & Tyler, 2000), one image set (set A) probed the coarse categorisation of everyday items as natural versus non-natural objects. This set comprised 60 images of natural objects (e.g, birds, mammals, and trees, mean pixel intensity 0.91 (0.06), mean contrast 0.22 (0.08)) and 15 images of non-natural objects (e.g. buildings, clothing, and furniture, mean pixel intensity 0.88 (0.06), mean contrast 0.25 (0.06))). A second set of images (set B) included only natural items and probed the more fine-grained classification of these items as animals versus non-animals (c.f Blundo, Ricci, & Miller, 2006; Hart & Gordon, 1992). Hence, it comprised 60 images of animals (e.g. mammals, birds, and marine animals, mean pixel intensity 0.91 (0.05), mean contrast 0.22 (0.06))) and 15 images of non-animals (e.g. fruit, vegetables, and nuts, mean pixel intensity 0.92 (0.05), mean contrast 0.19 (0.08)). The third set (set C), finally, contrasted different types of animals (c.f. Naselaris, Stansbury, & Gallant, 2012). Specifically, it contained images of 60 birds (e.g., blackbirds, budgies, and owls, mean pixel intensity 0.94 (0.06), mean contrast 0.18 (0.04)) with images of 15 non-birds (i.e., small mammals such as mice, rabbits, and squirrels mean pixel intensity 0.93 (0.02), mean contrast 0.19 (0.04)). As there were not enough bird images in the original Moreno-Martínez and Montoro image set, an additional 30 images were sourced using a Google image search and adapted to match the Moreno-Martínez and Montoro images in

relevant physical characteristics. All images were 250x250 pixels, 72dpi, subtending 9° visual angle, with the central image cropped to a white background. In order to reduce systematic low-level colour confounds between the standard and oddball categories all images were converted to greyscale. In addition, control images were created by box scrambling the original images using the Matlab Randblock function (https://uk.mathworks.com/matlabcentral/fileexchange/17981-randblock). Box scrambling has been shown to remove semantic category information content, whilst preserving low-level visual content (e.g. Grill-Spector et al., 1998). An example of the images is provided in Figure 1 and the full image set is available in Supplementary Information A.

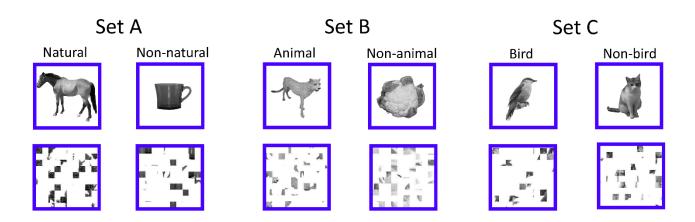


Figure 1: Examples of image sets and the equivalent scrambled control images.

2.3 Procedure

Participants were seated 55cm from the monitor and instructed to maintain their gaze within a blue fixation square in which images were presented. They were instructed to press a hand held button every time the blue fixation square turned green. Images were presented onscreen for 80ms with an interstimulus interval of 80ms. The study used an oddball paradigm presented in a steady state method as developed by Rossion and colleagues (e.g. Liu-Shuang et al., 2016; Rossion et al., 2015).

Images were presented in sequences of five images, with the first four images being selected from the standard category and every fifth image being drawn from the oddball category. An example of this sequence is presented in Figure 2. This design elicits two distinct steady state responses. The standard presentation frequency of 6.25Hz, and the oddball presentation frequency of 1.25Hz.

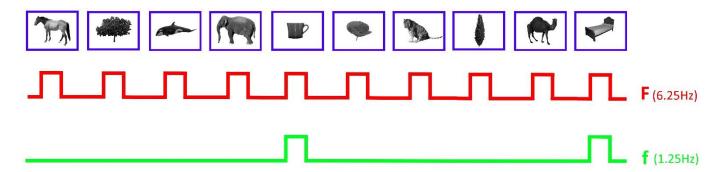


Figure 2: Oddball steady state design and hypothesised neural steady state responses. A base frequency \mathbf{F} is elicited in response to the presentation of every image at 6.25Hz, the oddball response \mathbf{f} is elicited only to stimuli that violate the previously established semantic category of the standard stimuli. In the example above the standard stimuli are living objects and the oddball stimuli are non-living objects.

Stimuli were presented in runs of 75 stimuli (60 standards and 15 oddballs) in a pseudo-randomised order ensuring 4 standard stimuli and a fifth oddball stimulus were always presented sequentially. Targets (fixation square turning green) only occurred on the second stimulus of the run of five, with a 10% probability of occurring for each run. This was repeated 15 times with a different randomised order each time resulting in 1125 stimuli presentations over 180s.

Six conditions were presented: Image Sets A, B and C and their equivalent scrambled control image sets.

The order of these blocks were counterbalanced across subjects using a balanced latin square design.

2.4 EEG recording

EEG signals were sampled at 1000Hz from 64 Ag/AgCl electrodes fitted on a standard electrode layout elasticised cap using a BrainAmp DC amplifier (Brain Products GmbH) with a common FCz reference and online low-pass filtered at 250Hz. Impedances were below $5k\Omega$. Recordings were analysed offline using Brain Electrical Source Analysis software v5.3 (BESA GmbH), Matlab (Mathworks Inc.) and the Fieldtrip toolbox (Oostenveld, Fries, Maris, & Schoffelen, 2011). Artifacts including blinks and eye movements were corrected using BESA automatic artifact correction (Berg & Scherg, 1994).

2.5 EEG analysis and Steady state response

Data were re-referenced offline to a common average reference. Epochs from 0 to 180s around block onset were defined for each condition. The steady-state response was calculated according to the procedures described in (Rossion et al., 2015). Epochs were defined as the entire 180 second trial period

associated with each semantic or control condition. This epoch length represents an integer number of cycles (225) of the oddball stimulus (1.25Hz) ensuring that a frequency bin corresponding to the exact oddball frequency and its harmonics, including the standard frequency (6.25Hz), were created. The frequency resolution was .0056Hz. Epochs were first linearly de-trended and the DC component was removed. The epochs were tapered with a Tukey window (matlab's tukeywin function) with the first and last 4 seconds of the epochs being cosine tapered in order to remove discontinuities at the edge of the epochs. For each participant and each electrode, amplitude was computed on these windows using the fast Fourier transform (FFT). Amplitude was then corrected by dividing the amplitude in each frequency bin by the mean amplitude of surrounding bins within a +/- 0.45Hz range (e.g. Alp et al., 2016; Srinivasan, Russell, Edelman, & Tononi, 1999) excluding the immediately adjacent bins (first neighbouring bin on each side). The +/- 0.45Hz range was chosen to give an amplitude correction that was comparable with previous research (e.g. Alp et al., 2016; Srinivasan et al., 1999), and represented 81 bins either side given the frequency resolution of this study. Excluding the immediately adjacent bins from this correction meant that the amplitude correction was less likely to include any spread of the fprs signal to proximal frequency bins (e.g. for 1.25Hz adjacent bins were 1.2444 & 1.2556Hz).

Previous research has shown a robust SSVEP response to the oddball frequency and many of its harmonics (e.g., Rossion et al., 2015; Norcia et al., 2015), so following the procedure outlined in Rossion et al. (2015) we determined the range of harmonics across which to analyse the data. Grand-average amplitudes (uncorrected) were created for each electrode and then pooled across all electrodes. The z-score for each frequency bin was then calculated using the mean and standard deviation of +/-0.45Hz bins, excluding the immediately adjacent bins (as described above). Harmonics of the oddball frequency in excess of z=3.29 (p<.001) were defined as significant (see Table 1). The harmonics used in later analysis were based on the largest range of consecutive and significant harmonics across all 6 presentation conditions. From 1.25Hz upwards (e.g. 2.5, 3.75, 5Hz...), once a harmonic failed to reach significance, we capped the range for that condition as the last harmonic that was significant. Harmonics that related to the standard frequency (e.g. 6.25Hz, 12.5Hz...) were excluded. Following the procedures of Rossion et al. (2015) and Heinrich et al.

(2009b) the corrected amplitude was calculated for 3 values: the standard frequency \mathbf{F} (6.25Hz), the oddball frequency \mathbf{f} , and the sum of the oddball frequency and significant harmonics \mathbf{f} + (i.e. sum of 1.25, 2.5, 3.75,5 & 7.5Hz). These three values were calculated for each participant and electrode across the six experimental conditions.

Using Fieldtrip software (Oostenveld et al., 2011), the difference in *f+* between original and scrambled images for the three levels of semantic categorisation was statistically assessed across all electrodes using cluster-based permutation analysis (see Maris & Oostenveld, 2007) with 10,000 permutations. For image Sets A and C the initial alpha value for cluster formation was lowered from alpha<0.05 to alpha<0.001, and for Set B it was lowered to alpha<0.01, as the difference was so large between experimental and control conditions that one large cluster spanning the entire scalp emerged. This is one weakness of the cluster permutation approach highlighted recently by Mensen and Khatami (2013). As a "sanity check" for the appropriateness of the cluster-based electrode selection a split-halves analysis was undertaken in which the subjects were split into two groups of 10. The 10 electrodes showing the strongest effect in subgroup 1 were then used to examine the experimental effects in the subgroup 2, and vice versa. All experimental effects were maintained and validate the cluster-based approach.

2.6 Presentation durations required to measure the steady state response

To examine the time required to detect a reliable steady state oddball response, the steady state response was calculated over 15 increasing epoch lengths from 12 to 180 seconds (12 second increments). All lengths included an integer number of cycles at the oddball frequency. The steady state response was calculated in a similar way to the procedure described in the previous section except that amplitude values were converted to z-scores using the mean and standard deviation of the frequency bins +/-0.45Hz (excluding the immediately adjacent bins). This allowed the significance of the steady state response at the oddball f, oddball plus harmonics f+, and standard frequency F to be assessed relative to alpha levels of 0.05 (z=1.96) and 0.001 (z=3.29), for a similar approach see (Rossion et al., 2015). The electrodes selected were those showing the largest f+ response (PO10 for image sets A and C, PO9 for image set B). For the group-level analysis, the across-participant mean z-score for each epoch length was then calculated for

each image set separately so that the detectability of the steady-state response to ${\it F}, {\it f}$ and ${\it f+}$ could be								
investigated over increasing lengths of stimulus presentation.								

3 Results

Fourier analysis of responses to the three image sets showed large steady state responses at 6.25Hz (*f*), 1.25Hz (*f*) and its harmonics at 2.5Hz, 3.75Hz, 5Hz and 7.5Hz (*f*+) (see Table 1). Cluster permutation analyses demonstrated significantly increased *f*+ for the all three image sets compared to scrambled controls, clearly demonstrating that *f*+ responses were not due solely to low-level visual differences but reflected deviance detection due to semantic categorisation differences.

		Condition					
Harmonic (Hz)	Set A	Set A	Set B	Set B	Set C	Set C	
		control		control		control	
1.25	5.07	2.65	6.02	3.36	3.45	1.53	
2.5	18.61	4.88	10.20	7.42	5.60	3.20	
3.75	23.05	7.75	12.61	6.99	19.99	5.63	
5	21.22	7.31	11.58	5.49	13.48	4.34	
7.5	3.54	1.87	10.78	6.06	5.98	3.77	
8.75	2.86	2.55	0.98	1.44	2.74	1.66	
10	2.62	3.65	1.05	0.71	0.21	2.05	
11.25	1.49	1.01	2.29	0.70	0.49	1.45	
13.75	2.09	0.94	0.90	0.39	0.16	-0.13	
15	0.21	1.04	-0.24	0.17	1.50	-0.68	
16.25	-0.46	2.46	-0.63	0.48	0.17	-0.22	

Table 1. Across participant z-scores at oddball frequency and its harmonic (scalp-average). Bold indicates significance at p<.001

3.1 Set A

Initial cluster analysis at cluster formation alpha<0.05 revealed one large cluster which included all electrodes. To identify the strongest areas of activity on the scalp, electrode clusters were formed with an entry alpha<0.001, which revealed a cluster with activity strongest in occipital and central areas including electrodes FCz, F4, FC5, FC1, FC2, FC6, T7, C3, Cz, C4, CP1, CP2, TP10, P8, P09, O1, Oz, O2, P010, F1, F2, FC3, FC4, C5, C1, C2, C6, CP3, CPz, CP4, TP8, P6, P07, P03, P04, P08, cluster p < 0.0001, see Figure 3.

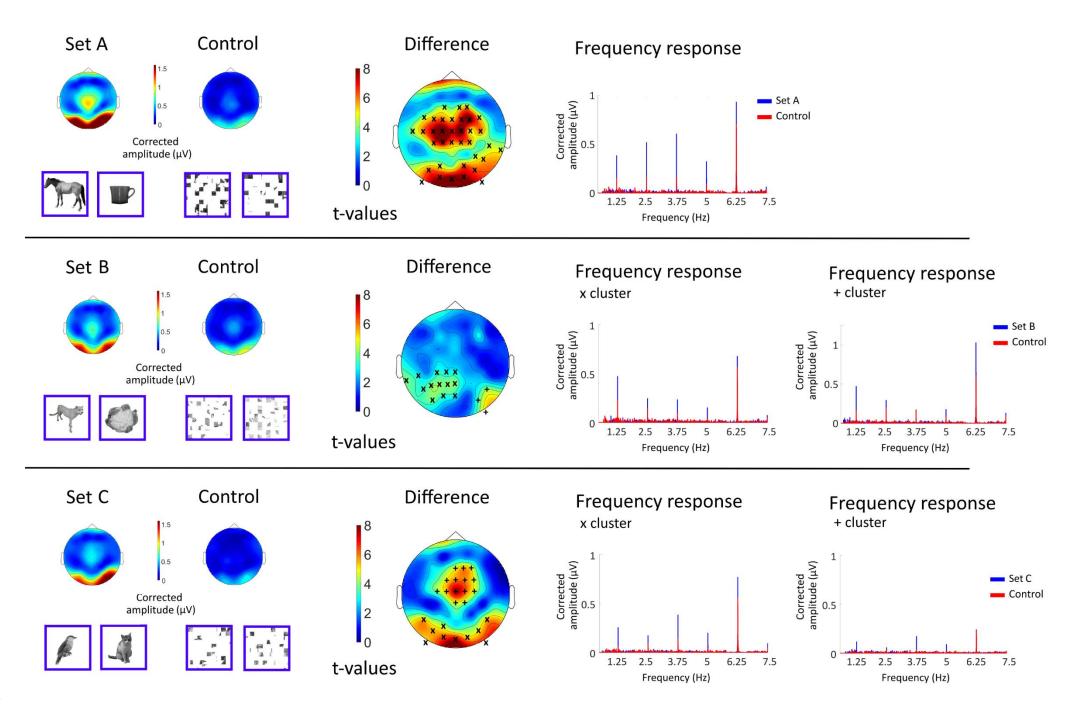
3.2 Set B

Cluster analysis at cluster formation alpha<0.01 revealed a left hemisphere dominant centro-parietal cluster comprising electrodes CP1, CP3, CPz, PO7, PO3, TP9, P7, P3, Pz, TP7, P5, P1, POz, cluster p < 0.001, and a right hemisphere dominant parieto-occipital cluster comprising electrodes P8, PO10 and PO8, cluster p = 0.008, see Figure 3.

3.3 Set C

Initial cluster analysis at cluster formation alpha<0.05 revealed one large cluster which included all electrodes. To identify the strongest areas of activity on the scalp cluster formation alpha<0.001 revealed an parieto-occipital cluster including electrodes P8, PO10, PO8, PO7, PO3, P7, PO9, O1, Oz and O2, cluster p < 0.0001, and a central cluster comprising electrodes CPz, F4, FC1, FC2, C3, Cz, C4, CP2, F2, FC4, C1, C2, FCz and Fz, cluster p < 0.0001, see Figure 3.

It was observed that \mathbf{F} reduced when images were scrambled. To verify that any reductions in \mathbf{f} + observed were due to the removal of semantic content (as opposed to simply being a consequence of image scrambling) the percentage change in \mathbf{F} from original to scrambled was calculated. The difference in \mathbf{f} + at electrode PO7 was then examined in a 1-way (original vs scrambled) repeated measures ANCOVA with percentage change in \mathbf{F} as a covariate. The \mathbf{f} + to scrambled images was significantly reduced image sets A (F(1,18)=35.64, p<0.001), B (F(1,18)=6.75, p<0.05) and C (F(1,18)=17.26, p<0.001) after controlling for the percentage reduction in \mathbf{F} from original to scrambled images.



- 2 Figure 3: Topography plots indicating significant differences between image sets compared to their scrambled controls in the spectral power of f+ (sum of
- 3 1.25Hz and its harmonics at 2.5Hz, 3.75Hz,5Hz and 7.5Hz) at regions of interest identified by cluster permutation analysis. Spectral plots represent the mean
- 4 corrected amplitude of the electrodes included in the clusters identified with **x** and **+** markers.

3.4 Presentation durations required to measure the steady state response

3.4.1 Group effects

The main analysis demonstrated a SSVEP to the oddball stimuli demonstrating the detection of a change in semantic categorisation that occurred during the 3 minute trial period. As a follow-up analysis, we investigated the presentation duration of the stimuli needed for the across-participant amplitude at the oddball frequency of experimental trials to be detectable as statistically significant. By analysing the Z score over increasing presentation durations, we were able to investigate the time necessary for a stable and measurable steady state response to occur, see Figure 4. The Z score of *F* was greater than p=0.001 after 30s in all three conditions. The Z score of *f+* in response to image set A was greater than p=0.05 after 36s and greater than p=0.001 after 72s. The Z score of *f+* in response to image set B was greater than p=0.05 after 72s and greater than p=0.001 after 168s. The Z score of *f+* in response to image set C was greater than p=0.05 after 48s and greater than p=0.001 after 96s. A 3-way repeated measures ANOVA (Set A, Set B, Set C) indicated no significant effect of image set on onset time of *F* F(2,38)=1.80, p=0.178, or *f+* F(2,38)=2.29, p=0.115. For image sets A and C the sum of 1.25Hz and the subsequent four harmonics (*f+*) was a stronger than 1.25Hz alone (*f*). In image set B they were equivalent.

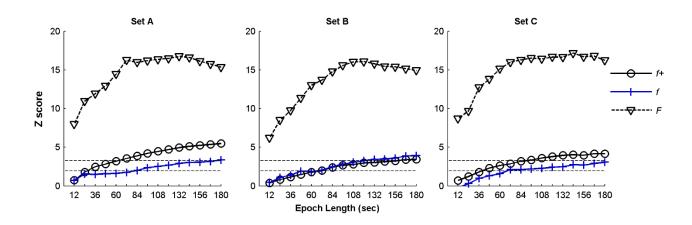


Figure 4: The F, f and f+ steady state responses over increasing presentation durations for image sets A and C at electrode PO10 and image set B at PO9. Z-scores reflect the deviation of amplitude at the specific frequencies of stimulation (F, f & f+) from surrounding frequencies (+/- 0.45Hz). The horizontal dashed lines indicate the z-score thresholds associated with conventional levels of statistical significance (z=1.96, p=0.05; z=3.29, p=0.001).

3.4.2 Individual subject effects

Analysis of individuals' amplitudes after increasing presentation durations demonstrated that the oddball *f+* response was detectable at a statistically significant (p<0.05) threshold in 1-2 mins for the majority of subjects. Figure 5 illustrates the distribution of individual subjects' times, individual values are available in Supplementary Info B.

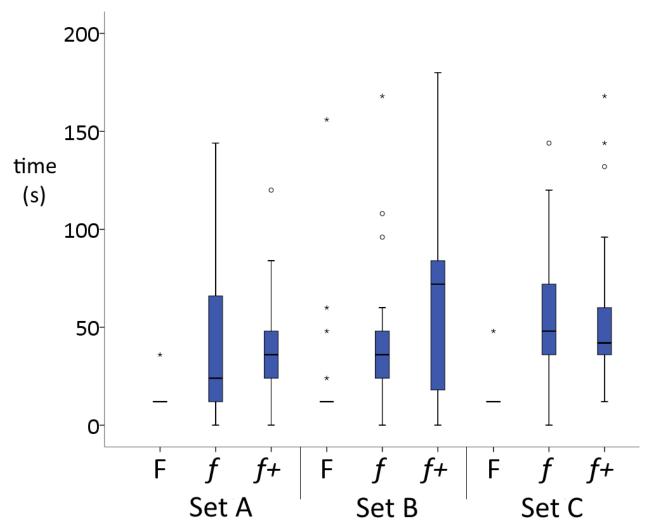


Figure 5: Time for individual subjects' F, f and f+ to reach z=1.96, p=0.05. Circles indicate subjects with times greater than 1.5 x Interquartile Range, asterisks indicate subjects with times greater than 3 x Interquartile Range.

4 Discussion

Across three levels of semantic categorisation subjects showed clear and distinct steady state responses to standard and oddball stimuli. Oddball responses were significantly increased compared to scrambled controls demonstrating that they were a result of a change in the semantic category of the visual object, and not due to systematic differences between standard and oddball stimuli in their basic visual properties or the overall reduction in steady-state responses to scrambled images. Examination of the amplitude of the oddball steady state responses after increasing presentation durations showed they were significant at group level at p<0.05 in under 72s in all three conditions. Individual subjects typically showed significant responses within ~60s. We have demonstrated that the FPVS-oddball paradigm is a powerful, sensitive and most importantly easily modifiable tool that can used to examine abstract conceptual processing in single subjects and groups.

The extension of this approach to abstract conceptual processing, e.g. semantic categorisation, is an important addition to the work of Rossion and colleagues in the field of face perception (e.g. Rossion, 2014). While the paradigm has also been demonstrated to be viable with lexical discrimination tasks (Lochy et al., 2015) ours is the first study demonstrating its validity in assessing abstract conceptual processing, e.g. semantic knowledge. There is considerable evidence for the ability of the visual system to classify objects after short presentation times during explicit target detection, e.g. during Rapid Serial Visual Presentation (Potter, 1975, 1976), and that classification can be made on the basis of higher level visual properties (e.g. VanRullen & Thorpe, 2001). Importantly however, we demonstrate that the FPVS-oddball paradigm is sensitive to implicit processing as participants were instructed simply to pay attention to all images presented and were not cued in any way to attend to the semantic category. Consequently, we are able to objectively measure the extent of pre-attentive discrimination without having to include the additional noise associated with the impact of masking and memory recall performance on explicit responses. The paradigm is therefore easily adaptable, and what constitutes an oddball and elicits an oddball response can be defined in low level visual or abstract conceptual properties.

We propose that the *f+* response in the current study reflects a combination of the visual MMN (vMMN) and a semantic category specific neural response. E.g. for image set A, the oddball response will reflect both change detection and the neural populations that respond specifically to non-living objects. These populations are stimulated at a rate of 1.25Hz, which we propose results in less neural habituation than in those being stimulated at 6.25Hz. Roving standard paradigms in traditional MMN studies have addressed the issue of neural habituation, and the extension of the FPVS-oddball paradigm to other oddball designs would be a worthy avenue for future investigation and may help to delineate the MMN response from that of differences in neural habituation.

The topographic distribution of responses to original images was broadly similar across the image sets, with the greatest power in lateral occipital sites, and a weaker but consistent central site. Scrambled images showed a considerably weaker but comparable pattern of lateral occipital and central activity. Cluster permutation analyses identified these areas as significantly different in both image sets A and C. The difference in in central areas is intriguing and points to neural generators beyond the visual cortex. The vMMN, which we propose forms part of the f+ response, has been demonstrated to involve neural generators in the Inferior Frontal Gyrus (Hedge et al., 2013). The temporal lobe, as part of the visual ventral stream, has repeatedly be shown to be involved in semantic categorisation (e.g. Anzellotti, Mahon, Schwarzbach, & Caramazza, 2010; Huth, de Heer, Griffiths, Theunissen, & Gallant, 2016; Kreiman, Koch, & Fried, 2000; Moss & Tyler, 2000). It is beyond the remit of the current study to make any claims about the neural generators of the oddball response but is certainly an avenue of interest for future studies, as the very high signal to noise ratio of the current approach would lend itself well to spatial modelling. While the topographies in response to original and scrambled images in image set B were similar to sets A and C, the cluster permutation analysis revealed a parietal and right hemisphere occipital cluster, which were less statistically significant than the clusters in sets A and C. It is possible that the distinction between standards and oddballs in set B was less clear than sets A and C, resulting in a weaker change detection response. This was neither anticipated or desired, but may be helpful in demonstrating the sensitivity of the approach to varying degrees of differentiation between standards and oddballs. MMN magnitude

increases as the difference between standards and oddballs increases (Näätänen, Pakarinen, Rinne, & Takegata, 2004; Pakarinen, Takegata, Rinne, Huotilainen, & Näätänen, 2007), therefore we maintain that although vMMN is not the sole driver of the *f+* response, the weaker vMMN to a standard-oddball pairing that is not as distinct as others may explain the difference in results. An alternative explanation is that the difference in topographies is due to different neural generators for the different semantic categories.

Dzhelyova et al. (2017) demonstrated distinct topographic patterns to different facial expressions using a similar FPVS-oddball technique. However we should be cautious in drawing immediate parallels between face and object processing, and further studies using a wide range of semantic categories is required to explore this possibility.

We have also demonstrated that the approach is remarkably stable and sensitive at the level of the individual subject, with most participants showing statistically significant oddball responses after only 60s. This has not been possible with traditional event-related paradigms, and resulted in an inability to translate promising experimental findings at group level to viable clinical tools at the individual level. In combination, the adaptability, speed, stability at the individual participant level, and sensitivity to implicit processing mean that with rigorous validation this approach has the potential to provide a reliable, objective, non-verbal measure of many aspects of cognition.

Finally, small **f+** responses were observed to the scrambled images. This was unexpected and is likely due to systematic differences in visual properties between the standard and oddball images that were not totally disrupted by box scrambling. E.g. in image set C birds vs non-birds feathers and fur would have been distinguishable even in the scrambled images. Additionally box scrambling created a small difference in the visual angle of the control stimuli as they were less concentrated in the centre of the fixation square. This highlights the need for the careful control of low-level visual characteristics when assessing higher level processing. Future studies should make every effort to ensure systematic differences are minimised, and investigate the efficacy of alternative techniques for generating control stimuli, e.g. phase, texture or diffeomorphic scrambling (Stojanoski & Cusack, 2014). Additionally future studies could include the reversal condition of standard and oddball stimuli, e.g. non-living objects as standards and living as

oddballs, in order to investigate any hierarchical preference in the visual system for particular semantic categories. While participants were not formally assessed for their explicit awareness of standard/oddball categories, anecdotally they indicated that they did not notice any change. Future studies should formally measure whether participants noticed any categorical change during the task, this would also allow direct comparisons with the Rapid Serial Visual Presentation literature.

In summary, we have demonstrated that the FPVS-oddball paradigm is a powerful new tool in cognitive neuroscience capable of being adapted to assess a wide range of cognitive functions. Stable and reliable at the level of the individual subject the technique has considerable clinical potential and provides an objective, non-verbal measure of abstract conceptual processing.

Acknowledgements

The authors would like to thank Bruno Rossion for the initial inspiration for this work and his subsequent advice and consultation.

6 References

- Alp, N., Kogo, N., Van Belle, G., Wagemans, J., & Rossion, B. (2016). Frequency tagging yields an objective neural signature of Gestalt formation. *Brain and Cognition*, 104, 15–24.
- Anzellotti, S., Mahon, B. Z., Schwarzbach, J., & Caramazza, A. (2010). Differential Activity for Animals and Manipulable Objects in the Anterior Temporal Lobes. *Journal of Cognitive Neuroscience*, *23*(8), 2059–2067. https://doi.org/10.1162/jocn.2010.21567
- Barsalou, L. W. (1991). Deriving categories to achieve goals. *Psychology of Learning and Motivation*, *27*, 1–64.
- Berg, P., & Scherg, M. (1994). A multiple source approach to the correction of eye artifacts.

 **Electroencephalography and Clinical Neurophysiology, 90(3), 229–241.

 https://doi.org/10.1016/0013-4694(94)90094-9
- Blundo, C., Ricci, M., & Miller, L. (2006). Category-specific knowledge deficit for animals in a patient with herpes simplex encephalitis. *Cognitive Neuropsychology*, *23*(8), 1248–1268.
- Bodatsch, M., Brockhaus-Dumke, A., Klosterkötter, J., & Ruhrmann, S. (2015). Forecasting Psychosis by Event-Related Potentials—Systematic Review and Specific Meta-Analysis. *Biological Psychiatry*, 77(11), 951–958. https://doi.org/10.1016/j.biopsych.2014.09.025
- Caramazza, A., & Shelton, J. R. (1998). Domain-specific knowledge systems in the brain: The animate-inanimate distinction. *Journal of Cognitive Neuroscience*, *10*(1), 1–34.
- Chan, A. M., Baker, J. M., Eskandar, E., Schomer, D., Ulbert, I., Marinkovic, K., ... Halgren, E. (2011). First-pass selectivity for semantic categories in human anteroventral temporal lobe. *Journal of Neuroscience*, *31*(49), 18119–18129.
- Chennu, S., Finoia, P., Kamau, E., Monti, M. M., Allanson, J., Pickard, J. D., ... Bekinschtein, T. A. (2013).

 Dissociable endogenous and exogenous attention in disorders of consciousness. *NeuroImage:*Clinical, 3, 450–461.
- Czigler, I. (2014). Visual Mismatch Negativity and Categorization. *Brain Topography*, *27*(4), 590–598. https://doi.org/10.1007/s10548-013-0316-8

- Duncan, C. C., Barry, R. J., Connolly, J. F., Fischer, C., Michie, P. T., Näätänen, R., ... Van Petten, C. (2009).

 Event-related potentials in clinical research: Guidelines for eliciting, recording, and quantifying mismatch negativity, P300, and N400. *Clinical Neurophysiology*, *120*(11), 1883–1908.

 https://doi.org/10.1016/j.clinph.2009.07.045
- Dzhelyova, M., Jacques, C., & Rossion, B. (2017). At a Single Glance: Fast Periodic Visual Stimulation

 Uncovers the Spatio-Temporal Dynamics of Brief Facial Expression Changes in the Human Brain.

 Cerebral Cortex, 1–18. https://doi.org/10.1093/cercor/bhw223
- Dzhelyova, M., & Rossion, B. (2014). Supra-additive contribution of shape and surface information to individual face discrimination as revealed by fast periodic visual stimulation. *Journal of Vision*, 14(14), 15–15.
- Erickson, M. A., Ruffle, A., & Gold, J. M. (2016). A Meta-Analysis of Mismatch Negativity in Schizophrenia:

 From Clinical Risk to Disease Specificity and Progression. *Biological Psychiatry*, *79*(12), 980–987.

 https://doi.org/10.1016/j.biopsych.2015.08.025
- Grill-Spector, K., Kushnir, T., Hendler, T., Edelman, S., Itzchak, Y., & Malach, R. (1998). A sequence of object-processing stages revealed by fMRI in the human occipital lobe. *Human Brain Mapping*, *6*(4), 316–328.
- Hart, J., & Gordon, B. (1992). Neural subsystems for object knowledge. Nature, 359(6390), 60–64.
- Hedge, C., Stothart, G., Jones, J. E., Frias, P. R., Magee, K., Leonards, U., ... Brooks, J. (2013). The neural generators of visual mismatch: a shared frontal generator across modalities (pp. 94–94). Presented at the Cognitive Neuroscience Society Annual Meeting, San Francisco: MIT Press 55 Hayward St, Cambridge, MA.
- Heinrich, S. P., Mell, D., & Bach, M. (2009a). Frequency-domain analysis of fast oddball responses to visual stimuli: A feasibility study. *International Journal of Psychophysiology*, 73(3), 287–293. https://doi.org/10.1016/j.ijpsycho.2009.04.011

- Heinrich, S. P., Mell, D., & Bach, M. (2009b). Frequency-domain analysis of fast oddball responses to visual stimuli: A feasibility study. *International Journal of Psychophysiology*, 73(3), 287–293. https://doi.org/10.1016/j.ijpsycho.2009.04.011
- Huth, A. G., de Heer, W. A., Griffiths, T. L., Theunissen, F. E., & Gallant, J. L. (2016). Natural speech reveals the semantic maps that tile human cerebral cortex. *Nature*, *532*(7600), 453–458. https://doi.org/10.1038/nature17637
- Kimura, M. (2012). Visual mismatch negativity and unintentional temporal-context-based prediction in vision. *Predictive Information Processing in the Brain: Principles, Neural Mechanisms and Models*, 83(2), 144–155. https://doi.org/10.1016/j.ijpsycho.2011.11.010
- Kreiman, G., Koch, C., & Fried, I. (2000). Category-specific visual responses of single neurons in the human medial temporal lobe. *Nature Neuroscience*, *3*(9), 946–953. https://doi.org/10.1038/78868
- Liu-Shuang, J., Norcia, A. M., & Rossion, B. (2014). An objective index of individual face discrimination in the right occipito-temporal cortex by means of fast periodic oddball stimulation. *Neuropsychologia*, 52, 57–72. https://doi.org/10.1016/j.neuropsychologia.2013.10.022
- Liu-Shuang, J., Torfs, K., & Rossion, B. (2016). An objective electrophysiological marker of face individualisation impairment in acquired prosopagnosia with fast periodic visual stimulation.

 Neuropsychologia, in press. https://doi.org/10.1016/j.neuropsychologia.2015.08.023
- Lochy, A., Van Belle, G., & Rossion, B. (2015). A robust index of lexical representation in the left occipitotemporal cortex as evidenced by EEG responses to fast periodic visual stimulation.

 Neuropsychologia, 66, 18–31. https://doi.org/10.1016/j.neuropsychologia.2014.11.007
- Mack, M. L., Gauthier, I., Sadr, J., & Palmeri, T. J. (2008). Object detection and basic-level categorization:

 Sometimes you know it is there before you know what it is. *Psychonomic Bulletin & Review*, *15*(1), 28–35.
- Monti, M. M., Vanhaudenhuyse, A., Coleman, M. R., Boly, M., Pickard, J. D., Tshibanda, L., ... Laureys, S. (2010). Willful Modulation of Brain Activity in Disorders of Consciousness. *New England Journal of Medicine*, *362*(7), 579–589. https://doi.org/10.1056/NEJMoa0905370

- Moreno-Martínez, F. J., & Montoro, P. R. (2012). An ecological alternative to Snodgrass & Vanderwart: 360 high quality colour images with norms for seven psycholinguistic variables. *PloS One*, *7*(5), e37527.
- Moss, H. E., & Tyler, L. K. (2000). A progressive category-specific semantic deficit for non-living things.

 *Neuropsychologia, 38(1), 60–82.
- Näätänen, R., Gaillard, A. W. K., & Mäntysalo, S. (1978). Early selective-attention effect on evoked potential reinterpreted. *Acta Psychologica*, *42*(4), 313–329. https://doi.org/10.1016/0001-6918(78)90006-9
- Näätänen, R., Kujala, T., Kreegipuu, K., Carlson, S., Escera, C., Baldeweg, T., & Ponton, C. (2011). The Mismatch Negativity: An Index of Cognitive Decline in Neuropsychiatric and Neurological Diseases and in Ageing. *Brain*, *134*(12), 3435–3453. https://doi.org/10.1093/brain/awr064
- Näätänen, R., & Michie, P. T. (1979). Early selective-attention effects on the evoked potential: A critical review and reinterpretation. *Biological Psychology*, 8(2), 81–136. https://doi.org/10.1016/0301-0511(79)90053-X
- Näätänen, R., Pakarinen, S., Rinne, T., & Takegata, R. (2004). The mismatch negativity (MMN): towards the optimal paradigm. *Clinical Neurophysiology*, *115*(1), 140–144. https://doi.org/10.1016/j.clinph.2003.04.001
- Naselaris, T., Stansbury, D. E., & Gallant, J. L. (2012). Cortical representation of animate and inanimate objects in complex natural scenes. *Journal of Physiology-Paris*, *106*(5), 239–249.
- Norcia, A. M., Appelbaum, L. G., Ales, J. M., Cottereau, B. R., & Rossion, B. (2015). The steady-state visual evoked potential in vision research: A review. *Journal of Vision*, *15*(6), 4–4. https://doi.org/10.1167/15.6.4
- Oostenveld, R., Fries, P., Maris, E., & Schoffelen, J.-M. (2011). FieldTrip: Open Source Software for Advanced Analysis of MEG, EEG, and Invasive Electrophysiological Data. *Computational Intelligence and Neuroscience*, 2011, 1–9. https://doi.org/10.1155/2011/156869
- Pakarinen, S., Takegata, R., Rinne, T., Huotilainen, M., & Näätänen, R. (2007). Measurement of extensive auditory discrimination profiles using the mismatch negativity (MMN) of the auditory event-related

- potential (ERP). *Clinical Neurophysiology*, *118*(1), 177–185. https://doi.org/10.1016/j.clinph.2006.09.001
- Potter, M. C. (1975). Meaning in visual search. *Science*, *187*(4180), 965–966. https://doi.org/10.1126/science.1145183
- Potter, M. C. (1976). Short-term conceptual memory for pictures. *Journal of Experimental Psychology:*Human Learning and Memory, 2(5), 509–522. https://doi.org/10.1037/0278-7393.2.5.509
- Rice, N. J., Valyear, K. F., Goodale, M. A., Milner, A. D., & Culham, J. C. (2007). Orientation sensitivity to graspable objects: an fMRI adaptation study. *Neuroimage*, *36*, T87–T93.
- Rogers, T. T., & Patterson, K. (2007). Object categorization: Reversals and explanations of the basic-level advantage. *Journal of Experimental Psychology: General*, *136*(3), 451–469. https://doi.org/10.1037/0096-3445.136.3.451
- Rosch, E. (1975). Cognitive representations of semantic categories. *Journal of Experimental Psychology:*General, 104(3), 192–233. https://doi.org/10.1037/0096-3445.104.3.192
- Rossion, B. (2014). Understanding individual face discrimination by means of fast periodic visual stimulation. *Experimental Brain Research*, *232*(6), 1599–1621. https://doi.org/10.1007/s00221-014-3934-9
- Rossion, B., Torfs, K., Jacques, C., & Liu-Shuang, J. (2015). Fast periodic presentation of natural images reveals a robust face-selective electrophysiological response in the human brain. *Journal of Vision*, *15*(1), 18.
- Srinivasan, R., Russell, D. P., Edelman, G. M., & Tononi, G. (1999). Increased synchronization of neuromagnetic responses during conscious perception. *The Journal of Neuroscience*, *19*(13), 5435–5448.
- Stojanoski, B., & Cusack, R. (2014). Time to wave good-bye to phase scrambling: Creating controlled scrambled images using diffeomorphic transformations. *Journal of Vision*, *14*(12), 6–6. https://doi.org/10.1167/14.12.6

- Tanaka, J. W., & Taylor, M. (1991). Object categories and expertise: Is the basic level in the eye of the beholder? *Cognitive Psychology*, *23*(3), 457–482.
- Tversky, B., & Hemenway, K. (1984). Objects, parts, and categories. *Journal of Experimental Psychology:*General, 113(2), 169.
- Umbricht, D., & Krljes, S. (2005). Mismatch negativity in schizophrenia: A meta-analysis. *Schizophrenia Research*, 76(1), 1–23. https://doi.org/10.1016/j.schres.2004.12.002
- VanRullen, R., & Thorpe, S. J. (2001). The Time Course of Visual Processing: From Early Perception to Decision-Making. *ResearchGate*, *13*(4), 454–61. https://doi.org/10.1162/08989290152001880