

The effect of the X-linked EFHC2 gene on social cognition and neural activation in healthy males

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Introduction

- Facial emotion expression recognition is important for social cognition. When we view faces distinctive ERP waveforms are produced, with the N170 wave corresponding to the structural encoding of faces (i.e. configural and holistic processing)
- The X chromosome may play a role in social cognitive abilities as ASDs (which are characterised by impaired social cognition) occur more commonly in males than females (3:1), and Turner Syndrome women (TS, X-monosomy) show impairments in facial emotion recognition
- In TS women, SNP rs7055196 on the EFHC2 gene (X chromosome, location Xp11.3) has been linked to fear recognition abilities; G allele (prevalence 9%) women were less accurate at facial fear recognition compared to A allele women (Weiss et al 2007)

Aim

- As both TS females and healthy males are X-monosomic, we investigated the effects of the different SNP rs7055196 variants on social cognition in males, specifically fear recognition abilities, gaze fixations to fearful faces and N170 amplitudes and latencies to fearful and angry faces

Methods

- Collected DNA samples from 567 healthy males and genotyped these to determine which variant of SNP rs7055196 males possessed
- Study 1: tested males (aged 18-40) with the G (n = 46) and A (n = 45) alleles on fear recognition abilities using faces morphed between fearful and neutral prototypes, also recorded fixations made to the faces (Figure 1, images from Fiorentini and Viviani 2009)
- Study 2: presented neutral faces (650ms) followed by fearful or angry faces (500ms) of different intensities (Figure 4) and recorded ERPs produced (G allele n = 17, A allele n = 12, age range 20-26)

Study 1: Method and Results

SNP rs7055196 influences facial fear recognition accuracy in males

- Participants viewed faces containing varying proportions of fearful and neutral expressions (0% to 100% fear with incremental steps of 10%) and had to decide which expression the face most resembled (Figure 1, 10 trials per face). This produced a psychometric function for each participant, from which fear recognition accuracy could be determined (Figure 2)



Figure 1. Examples of the morphed faces used to test fear recognition abilities (0%, 20%, 40%, 60%, 80%, 100% fear)

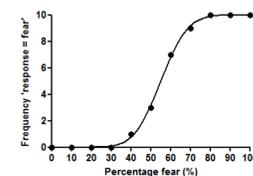


Figure 2. Example of the psychometric function produced; the gradient of the slope corresponds to fear recognition accuracy

- Males possessing the G allele were less accurate at fear recognition compared to males possessing the A allele (P = 0.042, effect size = 0.214, Figure 3)

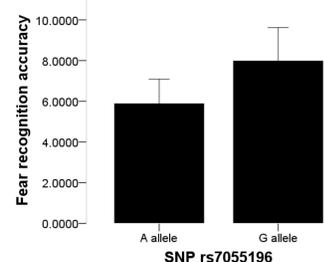


Figure 3. SNP rs7055196 significantly affected fear recognition accuracy (lower scores represent higher accuracy) ($t(89) = -2.067$, $P = 0.042$, 95% CI (-4.11, -0.08), A allele 5.88 ± 4.00 , G allele 7.98 ± 5.53) (error bars 95% CI)

SNP rs7055196 does not influence the total percentage of time spent fixating on the eye or mouth regions of faces in males

- There was no difference in the total percentage of time spent fixating the eyes and mouth of the faces used to investigate fear recognition accuracy between males possessing the G and A alleles (eyes $P = 0.831$, mouth $P = 0.551$)

Study 2: Method and Results

SNP rs7055196 influences N170 amplitude in males

- Participants passively viewed neutral faces followed by fearful or angry faces of varying intensities (low, medium and high, 40 trials each) (Figure 4) while continuous EEG was recorded



Figure 4. The morphed faces used to record ERPs to fearful and angry expressions (L angry, R fear, low, medium and high intensities)

- Males possessing the G allele produced smaller N170 amplitudes compared to males possessing the A allele (P = 0.028, effect size = 0.72, Figures 5 + 6)
- In addition, fearful faces produced greater N170 amplitudes compared to angry faces (P < 0.0005), while there was no effect of intensity level in the face (P = 0.430)

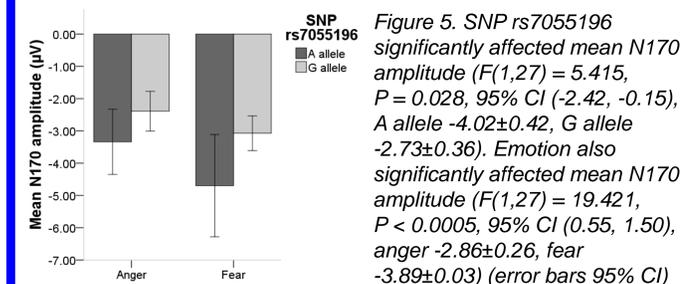


Figure 5. SNP rs7055196 significantly affected mean N170 amplitude ($F(1,27) = 5.415$, $P = 0.028$, 95% CI (-2.42, -0.15), A allele -4.02 ± 0.42 , G allele -2.73 ± 0.36). Emotion also significantly affected mean N170 amplitude ($F(1,27) = 19.421$, $P < 0.0005$, 95% CI (0.55, 1.50), anger -2.86 ± 0.26 , fear -3.89 ± 0.03) (error bars 95% CI)

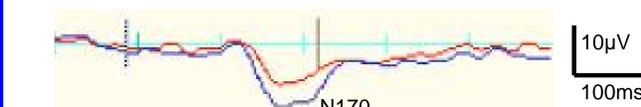


Figure 6. Average waveforms produced by males possessing the different variants of SNP rs7055196 for the fearful high intensity face (blue A allele, red G allele)

SNP rs7055196 does not influence N170 latency in males

- There were no differences in N170 latencies between males possessing G or A alleles (P = 0.212)
- Further, there were no differences in N170 latency for fearful and angry faces (P = 0.120) or for the different intensity levels (P = 0.496)

Conclusions

- Males possessing the G allele at SNP rs7055196 showed poorer facial fear recognition accuracy compared to males possessing the A allele. This was not due to a difference in fixation patterns
- Males possessing the G allele also showed smaller N170 amplitudes compared to those possessing the A allele when viewing fearful and angry faces
- The effect on N170 amplitude was much larger than that on fear recognition accuracy
- SNP rs7055196 may influence face processing style, as the N170 component is associated with the structural encoding of faces. Males possessing the A allele may use a more configural / holistic style (i.e. processing faces as a whole), while males possessing the G allele may use a more feature based style (i.e. processing facial features individually)
- The EFHC2 gene may play a role in the development of social cognitive abilities, and its location on the X chromosome may contribute towards explaining why impairments in social cognition occur more commonly in males compared to females. This gene may therefore be a candidate gene for the development of ASDs

References and Acknowledgements

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Weiss LA, Purcell S, Waggoner S, Lawrence K, Spektor D, Daly MJ, Sklar P, Skuse D (2007) *Hum Mol Genet* 16: 107-113

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