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Gender incongruence and the brain – Behavioral and neural correlates of voice gender perception in transgender people

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ABSTRACT

The phenomenon of *gender incongruence* is hypothesized to arise from a discrepant sexual development of the brain and the genitals, contingent on genetic and hormonal mechanisms. We aimed at visualizing transgender identity on a neurobiological level, assuming a higher functional similarity to individuals of the aspired rather than assigned sex. Implementing a gender perception paradigm featuring male and female voice stimuli, behavioral and functional imaging data of transmen were compared to men and women, and to transwomen, respectively. Men had decreased activation in response to voices of the other sex in regions across the fronto-parietal and insular cortex, while the activation patterns of women and transmen were characterized by little or no differentiation between male and female voices. Further, transmen had a comparatively high discrimination performance for ambiguous male voices, possibly reflecting a high sensitivity for voices of the aspired sex. Comparing transmen and transwomen yielded only few differences in the processing of male compared to female voices. In the insula, we observed a pattern similar to that of men and women, the neural responses of the transgender group being in accordance with their gender identity rather than assigned sex. Notwithstanding the similarities found dependent on biological sex, the findings support the hypothesis of gender incongruence being a condition in which neural processing modes are partly incongruent with one's assigned sex.

1. Introduction

Gender incongruence describes the condition of a strong and persistent discrepancy between one's assigned sex and psychological gender. Those affected are in discomfort with their anatomical sex and wish to live and be accepted as a member of the other sex. In the last few years the public and media have become more aware of transgender issues. The number of those affected is higher than previously thought, and they often face severe discrimination and are at risk for poor mental and physical health (Reisner et al., 2016; Winter et al., 2016). Many transgender individuals request for cross-sex hormonal treatment and gender confirmation surgery (World Health Organization, 2014). They can be given the clinical diagnosis of *gender dysphoria* (GD; *Diagnostic and Statistical Manual of Mental Diseases 5, DSM-5;* American Psychiatric Association, 2013) or *gender identity disorder* (GID; 10th revision of the International Statistical Classification of Diseases and Related Health Problems ICD-10; World Health Organization, 2014) if the condition causes psychological distress. There is an ongoing controversy surrounding these diagnoses, as many feel they suggest that any deviation from the male or female norm is pathological.

Gender incongruence is hypothesized to arise from a discrepant sexual development of the brain and the genitals, induced by genetic (Gómez-Gil et al., 2010; Heylens et al., 2012) and hormonal mechanisms (Kraemer et al., 2009; Schneider et al., 2006). For instance, a genetically determined altered sensitivity or function of sex hormone receptors or synthesis of sex steroids could lead to an anomalous exposure to sex hormones during fetal development. The fetal brain develops into a male brain under the influence of the androgen testosterone, and into a female brain in the absence of testosterone. As the sexual differentiation of the brain and the genitals occurs at different

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points in time, the two processes could be influenced independently, possibly resulting in gender incongruence when evolving in opposing directions (Bao and Swaab, 2011).

Studying the neurobiological correlates of gender incongruence enables unique insight into gender-based brain processes. In recent years, a growing number of studies have inquired into structural and functional correlates of gender incongruence, evincing the variance in sexual development and challenging the view of the brain as being strictly gender-binary. Although not all studies account for differences to cisgender (non-transgender) controls, many find the brain structures or activation patterns of transgender people to be closer to controls sharing their gender identity or to fall halfway between those of men and women (for a review see Smith et al., 2015).

The current work aims at visualizing transgender identity using a voice gender discrimination paradigm which evoked robust behavioral and neural activation differences between men and women in our previous study (Junger et al., 2013). Investigating voice gender perception in transgender people is of particular interest, as in the course of transition, many undergo voice training to adjust their voice to their aspired sex. The sexual dimorphism of the human voice mainly arises from anatomical differences: The male vocal folds and vocal tracts are generally longer in men, resulting in a lower fundamental frequency and closer spacing of formant frequencies. Voice gender categorization relies on the extraction of auditory features (e.g. pitch) along the superior temporal gyrus (Hickok and Poeppel, 2007; Lattner et al., 2005) and is carried out in interplay with the prefrontal cortex (Charest et al., 2013).

We found an *opposite-sex effect* for voice gender perception, reflected in higher accuracy, lower reaction times, a response bias and increased activation (or decreased deactivation) in frontotemporal regions in response to voices of the other sex (Junger et al., 2013). Men were more accurate and faster at identifying a voice as being female compared to male, and were biased to indicate a voice as being female rather than male. Further they showed higher activation (or less deactivation) for female compared to male voices in the orbitofrontal cortex, middle temporal gyrus and medial prefrontal cortex. The opposite was true for women. However, the effect was stronger or more robust in men compared to women, and more pronounced for gender-ambiguous voices (voice gender morphing).

Analogous effects have been reported for the visual domain, with less processing time for opposite-sex faces (Hofmann et al., 2006). The apparently higher sensitivity to characteristics of the other sex could be accounted for by an evolutionary relevance of selecting adequate mates, as suchlike stimuli convey information on a person's hormonal status (Feinberg, 2008). In transwomen (male-to-female transgender individuals), however, an opposite-sex effect for voice perception was not found. Compared to men and women, transwomen responding to male versus female voices exhibited activation differences in a network including the medial prefrontal gyrus, the insula, and the precuneus. When presented with gender-ambiguous voices, we found support for a more female-like processing mode, corroborating the lack of identification with their assigned sex (Junger et al., 2014). In the current study we compared behavioral and neural responses to male and female voices of different degrees of gender ambiguity between men, women and transmen (female-to-male transgender individuals). In addition, we exploratively compared the neural activation patterns of the transmen to those of (hormonally untreated) transwomen, described in Junger et al. (2014). Ensuing from our previous studies (Junger et al., 2014; Junger et al., 2013), we predicted the occurrence of an opposite-sex effect in men and women (albeit more pronounced in men), reflected in higher accuracy, lower reaction times (RTs) and a response bias for voices of the other sex. Correspondingly, we expected an interaction between voice gender and sex of the auditor in brain regions engaged in voice (gender) processing, such as the superior and middle temporal gyrus and parts of the (pre)frontal cortex. With increasing voice gender ambiguity, prefrontal and cingulate areas should be recruited due to higher cognitive demands.

In our previous study, transwomen, unlike men and women, showed a similar behavioral performance for male and female voices. Their brain activation patterns were different from those of men and women, and more similar to those of women in response to ambiguous voices (Junger et al., 2014). Hence, we expected transmen to show no clear behavioral preference for voices of either sex. Their activation patterns ought to be distinct from those of the women, and possibly converging to those of the men. In the exploratory comparison of transmen and transwomen, we were interested in seeing whether I) transmen and transwomen are similar with regard to behavior and brain activation, assuming that transgender individuals diverge from their assigned sex and converge to the other sex and thus “meet in the middle”, or whether II) the comparison elicits similar differences as between men and women, assuming that their activation patterns are in accordance with their gender identity (transmen resembling men and transwomen resembling women).

2. Materials and methods

2.1. Participants

Data of the heterosexual controls and transwomen were taken from our earlier studies described in Junger et al. (2014, 2013), applying the same paradigm. In addition, all participants performed a gender stereotype task and underwent structural MRI and resting-state fMRI. For the sake of reduced complexity, however, the results are presented elsewhere (e.g. Clemens et al., 2017). As more than half of the transgender individuals identified as homo- or bisexual, we attempted to balance the groups with regard to sexual orientation. Therefore, we included control men and women with mixed sexual orientation to obtain similar proportions of heterosexual and non-heterosexual controls (Table 1). The homosexual controls and transmen were newly recruited via LGBT organisations and self-help groups.

Exclusion criteria were neurological disorders, other medical conditions affecting the cerebral metabolism and axis I mental disorders (for the transgender groups: mental disorders unrelated to the transgender condition). None of the transgender participants reported to have undergone professional voice training and all participants were native German speakers. The data of four participants were discarded due to excessive movement in the MRI scanner (one heterosexual and one homosexual man, and two homosexual women). One transman was excluded from further analysis because of increased testosterone values (testosterone 39.60 nmol/l, free testosterone 105.5 pmol/l), suggesting the participant was taking steroids without reporting this or was suffering from a medical condition affecting testosterone levels.

In the final sample, behavioral and fMRI data of 18 transmen were compared to those of 19 cisgender men and women (56 individuals in total, Table 1). Additionally, the imaging data of the transmen were compared to those of 16 transwomen (34 individuals in total, Table 1). Four transmen reported the onset of the condition during childhood, one transman during early adolescence. For the majority of transmen, however, age of onset could not be reliably determined, as the information provided was either too vague or they could not accurately determine age of onset in retrospect. For the transwomen, information on age of onset was not available and could not be retrieved, as the sample had been collected from 2013 to 2014.

There were no significant differences in age between men and women ($t(36) = -0.88$, $p = .387$, $d = -0.29$), between men and transmen ($t(35) = 0.43$, $p = .670$, $d = 0.14$), or between women and transmen ($t(35) = 1.13$, $p = .266$, $d = 0.37$). The transwomen were significantly older than the transmen ($t(32) = -2.93$, $p = .008$, $d = -1.01$). There were no differences in educational level between men and women ($t(36) = 0.29$, $p = .774$, $d = 0.10$), between women and transmen ($t(33) = 1.86$, $p = .071$, $d = 0.61$), or between transmen and transwomen, respectively ($t(30) = -0.41$, $p = .685$, $d = -0.14$). Men had slightly more years of education than transmen ($t(33) = 2.46$, $p = .019$, $d = 0.81$).