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Inattention in misophonia: Difficulties achieving and maintaining alertness

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ABSTRACT

Introduction: Misophonia is marked by abnormal negative reactions to specific and idiosyncratic sounds. Despite unclear etiology and diagnostic conceptualization, neuropsychology may be able to help characterize the syndrome. In the current study, we administered the Attention Network Test (ANT) under symptom provocation conditions, as well as secondary measures of concept formation, perseveration, processing speed, and frustration tolerance. We assessed treatment seeking individuals with misophonia and non-clinical controls. We hypothesized higher alerting, orienting, and conflict effects on the ANT suggesting overall poorer performance for the misophonia group.

Methods: The sample consisted of symptomatic individuals recruited from a randomized treatment trial prior to the mandatory waitlist (n = 11) and age, gender matched controls (n = 11). Symptomatic individuals were screened with the Misophonia Questionnaire, as well as a number of additional self-report and diagnostic measures.

Results: Robust Bayesian estimation in multi-level models suggested worse alerting attention for symptomatic individuals, β_{Median} = 2.766, β_{SD} = 1.253, 95% *CI* [0.322, 5.2876], Bayes factor = 31.41. There were no effects respective to block (i.e., blocks before versus during and after symptom provocation) or interaction effects. There were also no effects particular to executive functioning measures but some evidence this domain should be further explored (e.g., ANT conflict effects, perseveration, and serial math accuracy).

Conclusions: We propose that symptom provocation alone does not explain the observed group difference in alerting attention, which could reflect a long-standing neuropsychological weakness. Future studies should attempt to characterize misophonia with more comprehensive neuropsychological batteries and larger samples.

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Misophonia, or selective sound aversion syndrome, is marked by abnormal negative reactions to specific and idiosyncratic sounds (e.g., eating/chewing, lip smacking, pen clicking, and clock ticking; Jastreboff & Jastreboff, 2015). Misophonia was first discussed in the audiological literature (Jastreboff & Jastreboff, 2001), although it differs from well-established disorders of decreased sound tolerance such as hyperacusis (i.e., generalized sound sensitivity; Aazh et al., 2014). Individuals with misophonia report negative reactions to a wide variety of sounds (Edelstein, Brang, Ramachandran, & Rouw, 2013; Schröder, Vulink, & Denys, 2013; Wu, Lewin, Murphy, & Storch, 2014), with no consistent pattern of cochlear abnormality or hearing threshold (Jastreboff & Jastreboff, 2015). Reactions vary, but typically include neurophysiological (e.g., tachycardia, angina, labored breath, tension headache, hyperthermia, diaphoresis) and affective-behavioral sequelae (e.g., fear, irritation, anger, disgust; Schröder et al., 2013; Schwartz, Leyendecker, & Conlon, 2011; Webber & Storch, 2015). At the time of writing, no study has systematically examined neurocognitive processes in misophonia. However, nine of eleven participants in Edelstein et al. (2013)'s sample complained that misophonia symptoms substantially impeded attention, and reported a benefit when attention was redirected from trigger stimuli. Therefore, neuropsychology may be able to contribute toward characterizing the syndrome.

Misophonia is not part of the *Diagnostic and Statistical Manual of Mental Disorder*s (5th ed.; DSM–5; American Psychiatric Association, 2013). Proposals have been made to classify it as a new disorder (see Dozier, Lopez, & Pearson, 2017; Schröder et al., 2013). However, it remains unclear whether taxometrically sound criteria can be established (e.g., whether symptoms pertain to psychology, neurology, audiology, or a combination of the three disciplines; Taylor, 2017). Misophonia shares commonalities with sensory intolerance, and perceptual anomalies such as synesthesia (Edelstein et al., 2013; Taylor, 2017). Studies assessing psychiatric overlap have been mixed,

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with some samples evincing corollaries to know diagnoses (e.g., obsessive compulsive and related disorders [OCRD] and post-traumatic stress disorder [PTSD]; Cusack, Cash, & Vrana, 2018; McKay, Kim, Mancusi, Storch, & Spankovich, 2018; Rouw & Erfanian, 2018), but no consistent pattern of co-morbidity (Frank & McKay, 2018; Schröder et al., 2013). Individuals with misophonia attempt to avoid situations that provoke symptoms, or inhibit symptoms when they occur, and show poor stress management (Edelstein et al., 2013; Frank & McKay, 2018). Several case reports and controlled trials have suggested preliminary support for psychosocial interventions (see Palumbo, Alsalman, De Ridder, Song, & Vanneste, 2018 for a review). To date, however, no treatment has been well validated with misophonia samples.

Not surprisingly given the nascent state of misophonia research, biological markers have proved elusive. Jastreboff and Hazell (2004) posited that enhanced auditory-limbic connectivity may be implicated. Kumar et al. (2017) found exaggerated blood-oxygen-level-dependent (BOLD) responses in the anterior insular cortex, elevated heart rate, and galvanic skin response (GSR) in participants with misophonia (n = 20) compared to age- and gender-matched controls. These differences were observed during participant responses to trigger sounds but not unpleasant or neutral sounds, and were associated with altered functional connectivity (during misophonia sounds only), greater myelination within the ventromedial prefrontal cortex (vmPFC), and greater self-reported awareness of bodily sensations. Similarly, Edelstein et al. (2013) reported elevated GSR during exposure to misophonia stimuli for participants with misophonia (n = 6) when compared to controls. Schröder et al. (2014) investigated event-related potentials (ERPs) and found a diminished N1 component (i.e., early attention to sensory changes) in participants with misophonia (N = 20). These findings provide initial support for neuro-biological correlates in persons who report the condition when exposed to trigger stimuli.

Neuropsychological functioning in misophonia

At the time of writing, only two studies have assessed neuropsychological functioning in individuals with misophonia. Eijsker, Schröder, van Wingen, and Denys (2018) administered a stop-signal task to 22 participants with misophonia and 19 controls. The misophonia group evinced intact response inhibition, but favored accuracy over speed, with concomitant BOLD hyper-activation of the superior medial frontal gyrus (SMFG) during inhibition failure and BOLD hypo-activation of the posterior cingulate cortex during success. Silva and Sanchez (2018) administered an adapted version of the Dichotic Sentence Identification Test (DSI; Andrade, Gil, & Iório, 2010) to participants with misophonia (n = 10), tinnitus (n = 10), and healthy controls (n = 20). Participants with misophonia showed significantly worse selective attention than other groups, but only when the DSI was administered with distractor stimuli (i.e., chewing sounds) rather than white noise. While few conclusions can be drawn due to the small number of studies, attentional processes in misophonia appear to warrant further investigation.

Posner and Petersen (1990) proposed attention as the composite of three interactive networks. Alerting attention, implicating right frontal and parietal regions, involves achieving and maintining sensitivity to incoming stimuli. Orienting attention, involving the superior parietal lobe, temporal parietal junction, and frontal eye fields, aligns attention to the source of sensory signals. Executive attention involves conflict monitoring and management, and implicates the midline frontal areas and lateral prefrontal cortex. The Attention Network Test (ANT), a computer-based application of the Eriksen flanker task, was designed to independently assess these three networks using alerting, spatial, and flanker cues (Fan, McCandliss, Sommer, Raz, & Posner, 2002). Consistent structural and functional imaging data have been found (Fan, McCandliss, Fossella, Flombaum, & Posner, 2005; Westlye, Grydeland, Walhovd, & Fjell, 2011), as well as data from studies using ERPs (Neuhaus et al., 2010). However, uncertainty remains regarding the independence of the attentional networks (see Macleod et al., 2010) and their relationship with executive functions (e.g., working memory capacity; Redick & Engle, 2006) .

The current study

The present study assessed neuropsychological functioning related to frontal systems in misophonia. This included a brief and targeted assessment of attention and executive functioning. Following Abramovitch and Schweiger (2015), we assumed that neuropsychological differences between symptomatic individuals and non-clinical controls would be in the small to moderate range. We also assumed that testing under conditions of symptom provocation would be informative. This is the first study to characterize misophonia using multiple neuropsychological instruments. Given the understudied nature of the syndrome, this attempt may provide an important basis for future efforts. This is also the first study to employ the ANT with a sample

reporting misophonia, and the first to modify the task to assess symptom provocation effects (see Methods). In order to further characterize frontal systems, we administered secondary neuropsychological and behavioral measures. We hypothesized that participants with misophonia would demonstrate higher alerting, orienting, and conflict effects on the ANT (of note, higher scores suggest worse attentional functioning). As an exploratory analysis, we assessed group effects in concept formation, perseveration, and frustration tolerance.

Method

Participants

We assessed participants with misophonia (n = 11) and matched controls (n = 11) in the current study. The groups were matched for gender (males = 4, females = 7), age, $F(1, 20) = 0.000$, $p = 1.000$, and years of education, $F(1, 20) = 0.026$, $p = .873$. All participants identified as non-Hispanic White except for one, who identified as biracial. The misophonia group was recruited from enrollees in a randomized treatment trial prior to the mandated waitlist period (see Frank & McKay, 2018). The treatment trial was designed to assess the efficacy of cognitive-behavioral interventions on misophonia symptoms. Participants were recruited via the misophonia Facebook page, postings on professional listservs, and through direct email contact by the principal investigator. All participants in the misophonia group reported at least moderate severity levels on the Misophonia Questionnaire prior to enrollment (MQ Severity Rating ≥ 7; Wu et al., 2014), and substantial functional distress related to the condition. While no established clinical criteria exist for a diagnosis of misophonia, the treatment seeking individuals in our misophonia group show qualitatively higher total MQ scores (M = 43.45, SD = 7.31) than our non-clinical control group (M = 12.27, SD = 8.15) as well as the community sample found in Wu et al. (2014; M = 17.81, SD = 9.17). Participants in the treatment trial were also screened for exclusion using the Structured Clinical Interview for DSM-5 (SCID-5; First, Williams, Karg, & Spitzer, 2015). Exclusion criteria for the treatment trial included significant cognitive impairment, autism spectrum disorder, psychosis, personality disorder, and past history of aggressive behavior, which were considered potential confounds for treatment efficacy. The current study was approved as an amendment to the treatment trial protocol. Of those participants enrolled during the active recruitment phase for the current study (n = 13), only two were unable to be matched with controls. One participant was determined to be ineligible based on exclusion criteria during this time period (namely, a diagnosis of autism spectrum disorder).

Instruments and procedure

In order to prevent uncontrolled symptom provocation from a human examiner, digitized and remote versions of all tests were administered. Attentional networks were assessed with the Attention Network Test (ANT; Fan et al., 2002). Participants completed 24 trial runs (with feedback) followed by 288 experimental trials. For each trial, arrows appeared either above or below a fixation cross with various flanker conditions pertaining to alerting, orienting, and conflict effects (respectively, no-cue versus double-cue, center-cue versus spatial-cue, and incongruent-cue versus congruent-cue). Participants were prompted to correctly identify the direction of each arrow. Effects were derived by subtracting mean response time between correct trials of respective conditions (see Fan et al., 2002).

Symptom provocation

The ANT was modified following a similar procedure to that found in Panagopoulos, Greene, Campbell, and Black (2013). Auditory stimuli were played during a randomized block (respectively, trials 1–96, 97–192, or 193–288), allowing a comparative index of performance (i.e., response differences for blocks before, during, and after auditory stimuli were played). Auditory stimuli consisted of recordings of sounds rated most aversive to a misophonia sample played in random order for 15s intervals (per Edelstein et al., 2013).

Additional measures

Perseveration, set shifting, and concept formation were assessed with the Wisconsin Card Sorting Test (WCST; Berg, 1948). Participants were asked to sort response cards according to an unknown matching principle, and adjust their approach during administration. A computerized version of the task was employed using 64 digital cards and responses were scored according to norms provided by Axelrod, Jiron, and Henry (1993).

Frustration tolerance was assessed with the Paced Auditory Serial Addition Task – Computerized (PASAT-C; Lejuez, Kahler, & Brown, 2003). In this task, participants were asked to complete serial math from sequentially displayed numbers. It was predicted that the stress management portion of the task would

be meaningful for our sample, and that the overall task would provide a secondary index of accuracy and processing speed.

Several self-report instruments were administered. Misophonia symptoms and behavioral reactions were assessed with the Misophonia Questionnaire (MQ; Wu et al., 2014). Depression, anxiety, and stress were assessed with the Depression Anxiety Stress Scale-21 (DASS-21; Lovibond & Lovibond, 1995). Anxiety sensitivity (i.e., the fear of sensations and behaviors associated with anxiety) was assessed with the Anxiety Sensitivity Inventory-3 (ASI-3; Taylor et al., 2007). Distress tolerance was assessed with the Distress Tolerance Scale (DTS; Simons & Gaher, 2005). Health and neurological histories were recorded using the Body Perception Questionnaire: Health History Inventory (Porges, 1993).

Participants provided written informed consent prior to enrollment in the study. The study was approved by the Institutional Review Board of Fordham University and conducted according to the principles of the Declaration of Helsinki. All participants were tested individually and given breaks between tasks. Participants completed self-report measures using the Survey Monkey Inc. platform (www.surveymonkey.com). Neuropsychological tests and instructions were administered digitally using Inquisit 5 (https://www.millisecond.com/). Participants were virtually monitored during testing with VSee (https://vsee.com/), a HIPAA-compliant video-chat interface. The entire research protocol lasted 120 minutes.

Statistical analyses

Analyses were conducted in the statistical programming language R (version 3.5.1; R Development Core Team, 2016). Linear models were first computed for demographic and self-report variables to assess effects between the misophonia and control group. In order to account for multiple comparisons in these analyses, a Bonferroni correction was employed (α = 0.01). Bootstrapped confidence intervals were computed using the *car* library with 10,000 samples (version 3.0–0; Fox & Weisberg, 2011).

For analyses pertaining to ANT data, an iterative process was employed (see Fox & Weisberg, 2011). A linear contrast model was computed using between subject (i.e., misophonia or control group) and within-subject factors (i.e., before versus during and after symptom provocation) for alerting, orienting, and conflict effects. Diagnostic plots were reviewed (e.g., residuals, Q-Q plots, etc.) and, when indicated, dependent variables were transformed using the *powerTransform* function in the *car* library. This function employs a maximum-likelihood-like approach to select an optimal univariate or multivariate transformation for linearity, normality, and constant variance (Box & Cox, 1964). For values with negative responses, a modification of the procedure was computed as designed by Hawkins and Weisberg (2017). Effect sizes were interpreted according to Cohen (1988) and Fritz, Morris, and Richler (2012).

Initial regression models for the ANT indicated possible violations of residual normality; therefore, transformations were employed (respectively, $\lambda_{Alerting}$ = 0.559, $\gamma_{Alerting}$ = 44.409; $\lambda_{Orienting}$ = 0.244, $\gamma_{Orienting}$ = 25.494; $\lambda_{Conflict}$ = 0.085, $\gamma_{Conflict}$ = 46.129). While these transformations were optimized from the given models, they also appeared to improve distortions at the univariate level (see Figure 1). However, all analyses were conducted employing transformed and non-transformed values and there were no differences in outcome.

In order to produce maximally reliable information from a small sample size, final models were assessed with robust Bayesian estimation, computed in the *rstanarm* library (version 2.13.1; Stan Development Team, 2016).

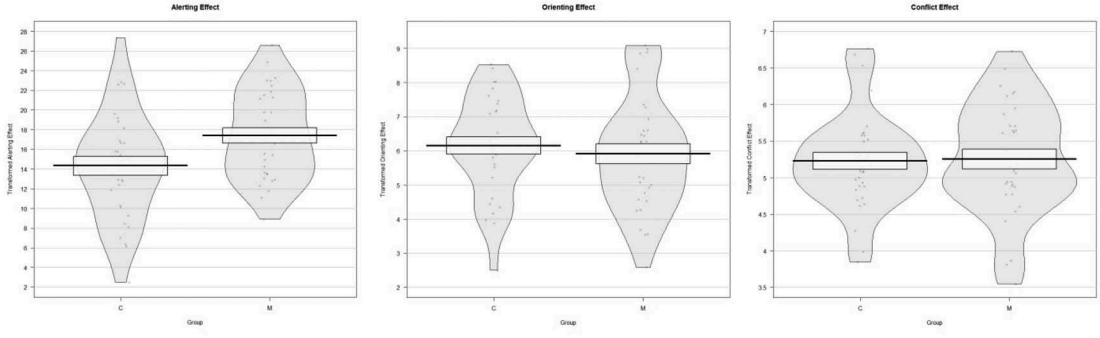

Figure 1. Attention network task data for misophonia and control groups. Plot includes the transformed data, mean, standard error, and smoothed density curve across all blocks of the task.

"C" represents the control group; "M" represents the misophonia group.

This algorithm produces Bayesian estimation of fixed effects using Markov chain Monte Carlo (MCMC) simulation with 10,000 iterations (Gelman & Hill, 2014). For all Bayesian models, default (weakly informative) priors were employed. Unlike null hypothesis testing, Bayesian models assess positive evidence for credible effects from the computed posterior distribution. Bayesian credible intervals provide an estimation of population parameters (versus an estimation of repeated sampling from a statistical distribution). Bayesian intervals are termed credible because they are an estimation of population values, a probability distribution of the "true value" for any given statistical question. This approach is less dependent on the sample, and any error contained therein, and more dependent on the "true value" having some predictable form (e.g., a specified prior). In the current study, it was assumed that the difference between groups was more likely null than negative or positive infinity. Since MCMC generation of the posterior distribution involves a unique and iterative process from the data (rather than repeated comparisons), and due to the robustness of these methods to Type I errors, no correction for repeated comparisons is necessary (Gelman, Hill, & Yajima, 2012; Jaynes, 2003; Wagenmakers et al., 2018).

For effects retained as credible, secondary Bayesian models were run estimating both fixed and random effects to assess any differences in outcome with this added parameter (i.e., group effects nested in the within-subject factor). Bayes factors were computed for retained effects with the *bridgesampling* library (Gronau et al., 2017) and interpreted according to Jeffreys (1998). Model fit was compared using leave-one-out cross-validation (LOO), the widely applicable information criterion (WAIC), and Pareto smoothed importance sampling (PSIS; see Vehtari, Gelman, & Gabry, 2017).

For additional neuropsychological measures, a similar procedure was employed. However, quit time on the PASAT-C was not assessed since exactly eight individuals (73%) from the misophonia and control groups completed the measure (i.e., a majority of both groups). We assessed a linear model comparing the total number of correct responses between the groups. For the WCST, we assessed linear models comparing standard scores for completed categories, total errors, and perseverative responses. Other data from the participants were reviewed qualitatively.

Results

As expected, the misophonia group reported higher levels of sound aversion and concomitant behavioral reactions than matched controls (see Table 1). There was a significant effect of group on the total score for this measure, $F(1,20) = 89.21$, $p < .001$, $\eta^2 = 0.82$, 95% *CI* [24.30, 38.07]. In addition, these participants reported significantly higher anxiety sensitivity, $F(1, 20) = 9.57$, $p = .005$, $\eta^2 = 0.324$, 95% *CI* [5.01, 25.72] and stress, $F(1, 20) = 13.75$, $p = .001$, $\eta^2 = 0.420$, 95% *CI* [6.14, 22.04], and lower distress tolerance than the control group, $F(1, 20) = 29.75$, $p < .001$, $\eta^2 = 0.598$, 95% *CI* [−34.19, −15.27]. Differences were observed in anxiety, $F(1, 20) = 5.95$, $p = .024$, $\eta^2 = 0.229$, 95% *CI* [1.13, 14.51] and depression, $F(1, 20) = 6.88$, $p = .016$, $\eta^2 = 0.266$, 95% *CI* [2.06, 18.31], which were not significant after Bonferroni correction ($\alpha = 0.01$).

Table 1. Demographic and self-report information for the misophonia and control group.

	Misophonia Group (n = 11)		Control Group (n = 11)	
	M (SD)		*M (SD)*	
Age	36.09	(12.01)	36.09	(12.33)
Years of Education	17.45	(2.58)	17.64	(2.69)
MQ: Symptoms	17.91	(4.85)	7.82	(5.36)
MQ: Behaviors	25.55	(5.47)	4.45	(3.47)
DASS-21: Depression	12.18	(12.08)	2.00	(2.11)
DASS-21: Anxiety	9.27	(10.48)	1.45	(1.81)
DASS-21: Stress	19.00	(11.56)	4.91	(4.85)
ASI-3	22.36	(15.86)	7.00	(4.45)
DTS	40.45	(14.67)	65.19	(3.30)

Means; standard deviations in parentheses. Anxiety Sensitivity Inventory-3 (ASI-3); Depression Anxiety Stress Scale-21 (DASS-21); Distress Tolerance Scale (DTS); Misophonia Questionnaire (MQ).

In addition, health and neurological histories suggested higher endorsement of some psychiatric and somatic complaints. A greater number of individuals in the misophonia group reported migraine headaches in comparison to the control group (18% versus 9%, respectively), as well as gastric/digestive problems (55% versus 18%), arthritis (27% versus 0%), hopeless unhappiness (9% versus 0%), depressive symptoms (36% versus 9%), back problems (27% versus 18%), gastric/duodenal ulcers (18% versus 0%), psychiatric disorders (18% versus 0%), and motion sickness (36% versus 9%). However, lower incidence of hypertension (0% versus 18%), anorexia (0% versus 9%), obesity (9% versus 27%), endocrine problems (0% versus 9%), diabetes (0% versus 9%), cancer (0% versus 9%), and pneumonia (0% versus 18%) were reported by the misophonia group.

In the initial models, the misophonia group evinced significantly worse alerting attention than the control group as suggested by a higher alerting effect, $\beta = 2.790$, $t(62) = 2.245$, $p = .028$, $d = 0.61$, 95% *CI* [0.4218, 5.200], when partialling out variance from within-subject effects (see Figure 1). The overall model was significant, $F(62) = 2.9109$, $p = .041$, $R^2 = 0.134$. This effect was consistent with robust Bayesian estimation in the final model, $\beta_{Median} = 2.304$, $\beta_{SD} = 1.204$, 95% *CI* [0.0109, 4.764], Bayes factor [BF] = 7.54. Further, the secondary, nested model

suggested an effect when partialling out variance from fixed and random within-subject effects, β_{Median} = 2.7766, β_{SD} = 1.253, 95% *CI* [0.322, 5.2876], BF = 31.41. While estimation was more precise in the nested model, model fit was relatively strong for both (WAIC = 405.6 and 406.0, *SE* = 12.8 and 12.9). All PSIS estimates were acceptable, suggesting little influence from outliers (Pareto *k*'s < 0.5).

In the initial frequentist model for alerting effects, there were no significant interaction effects and no significant within-subject effects from blocks during or after stimuli were played, β = 1.445, *t*(62) = 0.9658, *p* = .342, *d* = 0.17, and, β = 2.3766, *t*(62) = 1.5655, *p* = .125, *d* = 0.06, respectively. Likewise, there were no effects in the final Bayesian model, β_{Median} = 1.184, β_{SD} = 1.394, 95% *CI* [−1.5105, 4.0435] and, β_{Median} = 1.9876, β_{SD} = 1.460, 95% *CI* [−0.7766, 4.9329].

The initial model assessing orienting attention was not significant overall, *F*(3, 62) = 0.303, *p* = .823, R^2 = 0.03, or for between-subject effects, β = −0.2876, *t*(62) = −0.70698, *p* = .488, *d* = 0.16. Likewise, within-subject effects were not significant, β = 0.322, *t*(62) = 0.670, *p* = .506, *d* = 0.11, and, β = 0.280, *t*(62) = −0.5878, *p* = .566, *d* = 0.08. This was consistent with robust Bayesian estimation of between-subject effects in the final model, β_{Median} = −0.234, β_{SD} = 0.444, 95% *CI* [−1.2879, 0.6437]. Likewise, within-subject effects were not retained for orienting attention, β_{Median} = 0.283, β_{SD} = 0.5547, 95% *CI* [−0.7548, 1.5435], and, β_{Median} = 0.2435, β_{SD} = 0.542, 95% *CI* [−0.843, 1.500]. The initial model assessing the conflict effect was not significant overall, *F*(3, 62) = 0.4437, p = .727, R^2 = 0.02, or for between-subject effects, β = 0.0657, *t*(62) = 0.3215, *p* = .745, *d* = 0.02. Likewise, within-subject effects were not significant, β = −0.092, *t*(62) = −0.422, *p* = .674, *d* = 0.05, and, β = −0.2548, *t*(62) = −1.123, *p* = .266, *d* = 0.40. This was consistent with robust Bayesian estimation of between-subject effects in the final model, β_{Median} = 0.1878, β_{SD} = 0.744, 95% *CI* [−1.290, 1.70695]. Likewise, within-subject effects were not retained for the conflict effect, β_{Median} = −0.324, β_{SD} = 1.9986, 95% *CI* [−6.4877, 6.246], and, β_{Median} = −0.9326, β_{SD} = 1.9877, 95% *CI* [−7.070, 5.824]. None of the interaction effects in the orienting and conflict effect models were significant or retained.

Qualitative information on the ANT can be viewed in Table 2. There was a notable diminution in accuracy for the misophonia group across ANT stimuli. There was, however, a possible ceiling effect on this metric as both groups were highly accurate. Mean response time appeared to follow expected patterns for both groups, with more difficult ANT conditions provoking slower responses.

As noted, quit time on the PASAT-C was not assessed given that only three individuals (27%) from each group quit the task. There were, however, no significant differences in the total number of correct items for either raw, β = −8.6545, *t*(20) = −0.2655, *p* = .801, *d* = 0.11, or transformed (λ = 0.9409, γ = 356.9999) data, β = −54.00998, *t*(20) = −0.2876, *p* = .785, *d* = 0.12. This was consistent with robust Bayesian estimation for both raw, β_{Median} = −15.601, β_{SD} = 33.3219, 95% *CI* [−84.2108, 53.065], and transformed data, β_{Median} = −8.387, β_{SD} = 17.743, 95% *CI* [−43.930, 28.025]. On average, the control group answered slightly more items correctly than the misophonia group (M_{Miso} = 215.90, SD_{Miso} = 74.85; M_{Con} = 224.55, SD_{Con} = 84.01). Regarding the WCST, there were no significant effects between groups for completed categories, β_z = 0.208, *t*(20) = 0.511, *p* = .615, *d* = 0.22, total errors, β_z = −0.115, *t* (20) = −0.359, *p* = .723, *d* = 0.15, or perseverative responses, β_z = 0.325, *t*(20) = 1.059, *p* = .302, *d* = 0.45. These results were consistent with robust Bayesian estimation for completed categories, $\beta_{MedianZ}$ = 0.276, β_{SDZ} = 0.396, 95% *CI* [−0.521, 1.064], total errors, $\beta_{MedianZ}$ = −0.039, β_{SDZ} = 0.321, 95% *CI* [−0.675, 0.630], and perseverative responses, $\beta_{MedianZ}$ = 0.377, β_{SDZ} = 0.293, 95% *CI* [−0.227, 0.917].

Table 2. Proportion of correct responses and mean response time.

	Misophonia Group (*n* = 11)		Control Group (*n* = 11)	
	M	*(SD)*	*M*	*(SD)*
Proportion Correct				
No Cue	0.968	(0.064)	0.994	(0.014)
Center Cue	0.963	(0.049)	0.993	(0.016)
Double Cue	0.960	(0.082)	0.988	(0.022)
Spatial Cue	0.976	(0.048)	0.996	(0.013)
Congruent	0.975	(0.069)	0.996	(0.011)
Incongruent	0.944	(0.075)	0.986	(0.020)
Mean Response Time				
No Cue	576.79	(109.20)	568.18	(87.11)
Center Cue	531.64	(108.68)	538.42	(101.15)
Double Cue	512.40	(105.01)	528.47	(105.76)
Spatial Cue	491.23	(92.31)	495.06	(91.87)
Congruent	506.41	(99.32)	519.90	(95.11)
Incongruent	584.79	(114.26)	593.72	(115.02)

Means across blocks of the Attention Network Task (Fan et al., 2002); standard deviations in parentheses.

Discussion

This was the first study to attempt to characterize neuropsychological functioning related to frontal systems in misophonia using multiple neuropsychological instruments. Misophonia remains an under-studied condition, with unclear etiology and rudimentary diagnostic conceptualization (Brout et al., 2018; Cavanna & Seri, 2015; Palumbo et al., 2018; Taylor, 2017). Given the cross-sectional nature of this study, we cannot conclude whether observed differences between participants with misophonia (*n* = 11) and

matched controls (n = 11) reflect a long-standing neuropsychological weakness. However, our symptom provocation paradigm suggests this possibility. Our data indicate that the misophonia group had difficulties achieving and maintaining alertness during the attention task. The findings were consistent between frequentist models and nested models using robust Bayesian estimation. Bayes factors suggested the evidence for the effects was substantial (greater than 5) to strong (greater than 10). It is notable that effects respective to block, as well as interaction effects, were not retained in the overall model (i.e., blocks before versus during and after symptom provocation). This suggests that performance differences were not exclusively a result of symptom provocation (i.e., an impact on performance after stimuli were played). We propose that the observed group difference in alerting attention could be characteristic of individuals with misophonia. However, it would be warranted to administer a "cold" version of the ANT to similar participants in order to further support this finding.

Given the current results, we speculate that attentional disturbance in misophonia samples will be in the small to moderate range, even under symptom provocation conditions. Both groups showed an error rate similar to that found in previous studies using the ANT (e.g., Fan et al., 2002). However, there was somewhat worse accuracy for the misophonia group compared to matched controls across stimuli and conditions of the ANT. This feature contrasts somewhat with Eijsker et al. (2018). Of note, however, the stop-signal task employed in this study reflects successful engagement of a different cognitive capacity. Therefore, accuracy on various neuropsychological instruments may be an area that warrants further exploration.

Contrary to our hypothesis, we did not find differences in orienting attention, which aligns attention to the source of sensory signals. Enhanced resting auditory-limbic connectivity in persons with misophonia (as suggested by Jastreboff & Hazell, 2004; Palumbo et al., 2018) may entrain a strengthened orienting reaction to appraise stimuli for threat potential. However, further studies will be needed to confirm this result, and explore biological corollaries as well as clinical implications. In addition, we found no effects particular to executive functioning measures (e.g., ANT conflict effects, WCST perseveration, and PASAT accuracy). As such, our sample did not evince meaningful executive dysfunction. These data correspond with Eijsker et al. (2018)'s finding of intact response inhibition. However, given the medium effect size we documented on the WCST (i.e., perseverative responses), future studies should explore similar metrics.

While individuals with misophonia may have higher rates of diagnosable conditions, they have not shown a consistent psychodiagnostic pattern for comorbid or co-occurring disorders (Frank & McKay, 2018; Kumar et al., 2017; Schröder et al., 2013). In the current study, participants in the misophonia group endorsed higher levels of some psychiatric and somatic complaints than the control group, but no general pattern of poor health. We did not statistically control for substance use, anxiety, or depression in the current study. However, qualitatively, our participants reported anxiety and depression symptoms as a result of misophonia triggers, as well as their inability to exert control over their reactions. Similarly, participants reported that substance use was a coping mechanism for their symptomology. For this reason, partialling out variance in the models we used would be problematic (see Spector & Brannick, 2011). Of note, all of the participants in the misophonia group enrolled with misophonia as their primary complaint. In addition, to the best of our knowledge, there is no evidence that misophonia reactions are common sequelae of a primary mood or substance use disorder.

More studies will be needed to determine whether the clinical patterns in individuals with misophonia differ for those with and without co-occurring disturbances (e.g., through propensity score matching techniques; Lee & Little, 2017). However, we speculate that severe misophonia will typically be accompanied by affective disturbance and problematic coping behaviors. Therefore, we suggest that the current results are generalizable to persons with the condition. Longitudinal studies during symptom onset could help distinguish whether inattention plays some role in the etiology of misophonia, occurs as a result of symptoms, or derives from secondary effects (e.g., depression, anxiety, and substance use). We propose that difficulties achieving and maintaining alertness may create a state whereby aversive stimuli are poorly predicted, and given higher salience on occurrence. In addition, individuals with misophonia may have weaker capacities for autogenic redirection and distraction.

Studies have associated attentional dysregulation with audiological conditions such as tinnitus (Hallam, McKenna, & Shurlock, 2004; Roberts, Husain, & Eggermont, 2013). Following Roberts et al. (2013), Silva and Sanchez (2018) suggested that selective attention failures limit the allocation of perceptual processing resources in individuals with misophonia. Further, poor auditory gating and sensory over-responsivity (SOR) may be associated with deficits in predictive coding (a top-down process; see Pelt et al., 2016). This difficulty anticipating and coding incoming sensory information may account for the aberrant ERP

responses documented in misophonia samples (e.g., Schröder et al., 2014). Sensory over-responsivity could also explain the previously mentioned overlap with psychiatric conditions (Cavanna & Seri, 2015). As was suggested by Taylor (2017), misophonia may be a subcategory of SOR conditions.

Individuals with difficulty inhibiting their reactions to trigger stimuli, and diminished ability to redirect their attention, may show poor management of concomitant stress. For example, Bardeen, Tull, Dixon-Gordon, Stevens, and Gratz (2015) found that for participants with lower attentional control, reported emotion dysregulation corresponded with poor performance on a distress tolerance task. In misophonia, this same pattern could produce avoidance (a negative functional quality) and prevent adaptation to stimuli encountered in daily life (Frank & McKay, 2018). Attentional resources processed in the anterior insula have previously been linked to interoception, learning, error processing, and resultant anxiety sensitivity (see Paulus & Stein, 2006). Both anterior insula activity (Kumar et al., 2017) and anxiety (Wu et al., 2014) may have critical functions in misophonia. Understanding the neuropsychological profile of misophonia may help disentangle symptom etiology and provide guidance on the condition's functional impact.

The limitations of the current study include a small sample, and the lack of a comprehensive neuropsychological battery. In order to best optimize our data, we employed an iterative analytic procedure relying on advanced statistical methodology (i.e., Bayesian estimation via MCMC simulation). These methods have been documented as among the superior approaches to fitting multi-level models (see Browne & Draper, 2006; Shor, Bafumi, Keele, & Park, 2017). In addition, while our sample was comparable in size to some prior studies of misophonia (e.g., Edelstein et al., 2013), it was smaller than others (e.g., Kumar et al., 2017), especially studies conducted in the context of a specialized clinic (Jastreboff & Jastreboff, 2014; Schröder, Vulink, van Loon, & Denys, 2017). We cannot rule out the possibility of Type-II errors given this study's limited sample. In addition, sounds were played continuously, rather than time-locked to trial events (i.e., stimuli on the ANT). It is possible that participants predicted the time-interval used in the current study (15s), which dampened their distressing potential. We consider this unlikely given the random order of sounds played, their short duration, and qualitative reports that the exposure was distress-provoking. However, our results may reflect general rather than competing effects of misophonia symptoms. We employed this methodology in order to achieve ecological validity of the effects, since misophonia stimuli are typically experienced as continuous and asynchronous with task events. However, studies employing time- and phase-locked stimuli may provide important insights into the condition. The strengths of the current study include a novel methodology that enabled the examination of attentional functioning and symptom provocation effects.

Due to the constraints and time demands of our treatment protocol, we did not offer a full neuropsychological battery. However, there could be great value in comprehensively characterizing misophonia. In addition, assessing attentional networks under symptom-neutral conditions will be necessary to determine whether alerting difficulties relate to symptom-specific or generalized cognitive patterns. It may also be useful to compare visual and auditory modalities of the ANT (see Callejas, Lupiàñez, Funes, & Tudela, 2005). This was a cross-sectional study with several limitations. We cannot conclude whether misophonia symptoms were the specific cause of difficulties in alerting attention, or whether these difficulties reflect a long-standing weakness. However, given the current results, attentional vigilance should be an important feature for future studies of misophonia to examine.

Disclosure statement

No potential conflict of interest was reported by the authors.

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