Psychophysiological Indicators of Multisensory Processing in Autism Spectrum Disorder and Typical Development: A Pupillometry Study

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Abstract

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by impairments in social communication and interactions (APA, 2013). Pupillary responses are a reliable indicator of cognitive operations including preference, mental load, and emotional arousal. The current study utilized pupillary responses to dynamic, audio-visual stimuli to infer cognitive processes involved in perception of social and non-social stimuli, as well as to temporally manipulated (i.e., asynchronous auditory and visual presentations) stimuli. The current study had four main research objectives: 1) to characterize pupillary responses to social and non-social information in ASD and typical development (TD), 2) to characterize responses to asynchronous and synchronous audio-visual stimuli in ASD and TD, 3) to determine whether pupillary responses can accurately predict membership to the ASD or TD group, and 4) to understand the relationship between pupillary responses and measures of ASD symptoms and social factors.

Chronological and mental age-matched participants included 39 children with ASD and 32 typically developing children. Pupillary responses to social (Social-Linguistic, Social Non-Linguistic, and Social-Emotional) and non-social (Non-Social, Non-Linguistic) conditions were captured and recorded using an eye-tracker. Results yielded several key findings indicating differences between groups: 1) individuals with ASD demonstrated an attenuated pupillary response to social information, but not to non-social information, 2) in ASD, a reduction in pupillary response to social information was associated with greater impairments in social abilities and sensory processing as rated by caregivers, and 3) pupillary responses to social information was used to reliably predict group membership for children with ASD. Finally, this study did not observe between group differences in temporal processing, rather, both groups showed greater pupillary response to audio-leading asynchronous conditions, except for social-emotional conditions in which there was a significantly greater response to synchronous presentations. Results are discussed within the context of the engagement/arousal hypothesis of pupil dilation and the social motivation theory of ASD. Results are interpreted as evidence that reduced orienting to and under-engagement with social stimuli are implicated in the social impairments observed in ASD. This study demonstrates the usefulness and feasibility of pupillary response as a possible identification tool of the atypical social processing observed in ASD.

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Introduction

A growing body of literature supports the notion that individuals with autism spectrum disorder (ASD) have multisensory experiences that are distinct from those with typical neurological development (Iarocci & McDonald, 2006). Further, an increasing appreciation for atypical sensory experiences in ASD has been reflected in the current version of the Diagnostic and Statistical Manual of Mental Disorders, which now includes unusual reactions to sensory input as part of the core diagnostic features of the disorder (American Psychiatric Association, 2013). In addition to a tendency for hyper- or hypo-sensitivity to sensory aspects of the environment, described as part of restricted and repetitive patterns of behavior, individuals with ASD also have impairments in social communication and peer interactions (APA, 2013). Recent inquiry into the sensory experiences of individuals with ASD reveals a more complex issue than heightened or dulled sensory perceptions. Rather, factors related to the relative influence of competing sensory information, timing, and the nature of the multisensory event (e.g., speech, moving objects) appear to be involved in the processing of multisensory experiences in individuals with ASD (Bebko, Weiss, Demark, & Gomez, 2006; Smith & Bennetto, 2007; Stevenson, et al., 2014c). Insight into the underlying cognitive processes at play during speech perception is necessary to properly understand the socio-communicative deficits observed in ASD. Pupillary responses (patterns of pupil constriction and dilation) are one way to infer cognitive operations related to mental processing and arousal. The following sections are a brief introduction to multisensory integration in ASD and make the case for examining multisensory integration using psychophysiological data (i.e., pupillary response).

Multisensory Integration in ASD

A primary task of development is the ability to process and perceive incoming sensory signals to begin to make sense of the world. The ability to accurately combine what is *seen* with what is *heard* is a critical task for our survival in the environment, but also within our social surroundings. For example, the task of pairing the sound of screeching tires with an oncoming car may have very real implications, as will pairing the sound of our mother's voice with the image of her face. While the former example has potentially life-threatening consequences, the latter has consequences that relate to an individual's trajectory of social functioning throughout their lives; a critical element of our wellbeing as humans. It is known that within the first few months of life, infants begin to use the cues within their environments to accurately pair faces with voices (Kuhl & Meltzoff, 1984; Lewkowicz, 2010; Mendelson & Ferland, 1982) and match objects with their corresponding sounds, such as the sound of a ball hitting a table (Bahrick, 1992; Bahrick, Netto, & Hernandez-Reif, 1998).

Multisensory integration is a process that is fundamental to speech perception and has significant social implications. Speech is not only auditory, but also visual; seeing a speaker's face greatly improves speech communication (Sumby & Pollack, 1954). In order benefit from the process, one must properly integrate auditory and visual signals; a developmental process that begins in the first moments of life. This integrative process is taken advantage of in the nearly ubiquitous manner in which parents speak to their babies, using infant-directed speech, also known as "motherese." This type of parent-to-infant communication style provides exaggerated articulation, intonation, and facial movements, facilitating the learning of how speech signals should be bound together (Cooper & Aslin, 1990). Infants with ASD, however, show a significant decrease in time spent attending to other's faces (Osterling & Dawson, 1994), and may be less able to benefit from these interpersonal interactions.

The impact of multisensory integration on perception is demonstrated well by a phenomenon known as the McGurk effect. Specifically, the McGurk effect illustrates how multisensory processing is an active, dynamic process distinct from unisensory processing, and shows how the presence of multiple sensory inputs alters perceptual experience (MacDonald & McGurk, 1978). To elicit this phenomenon, an individual is presented with the audio recording of a person speaking the syllable "ba" but see the speaker visually articulating the syllable "ga." When incongruous auditory and visual stimuli are presented simultaneously, individuals often report that they perceive the speaker as having said "da" or "tha," syllables that were not present in either the auditory or the visual sensory inputs. Thus, what is perceived is a unified *fusion* of the two sensory modes. The McGurk effect demonstrates how multiple sensory inputs, when occurring at the same time, greatly shape our perception of the world around us beyond the mere linear combination of sensory inputs, resulting in a qualitatively different perceptual experience.

Interestingly, infants and children with ASD do not appear to integrate multisensory information with the same accuracy and efficiency as typically developed (TD) children. Individuals with ASD report the McGurk illusion *less* than their TD peers (Bebko, Schroeder, & Weiss, 2014; de Gelder, Vroomen, & van der Heide, 1991; Williams, Massaro, Peel, Bosseler, & Suddendorf, 2004), suggesting that multisensory information is not being integrated efficiently, but rather perceived as distinct sensory units. A similar phenomenon, the *speech detection advantage,* is based on the notion that visual information (e.g., seeing the speaker's face) invariably enhances an individual's ability to perceive or "hear" auditory speech (Grant & Seitz, 2000). However, individuals with ASD appear to benefit *less* from the presence of visual information than TD individuals (Smith & Bennetto, 2007) and rely more heavily on auditory information (Bebko et al., 2014; Iarocci, Rombough, Yager, Weeks, & Chua, 2010; Mongillo et al., 2008; Stevenson et al., 2014c) demonstrating an impairment in the perceptual integration of multisensory information in ASD. The implications of this type of impairment are profound, and are in line with the communication and social impairments observed in ASD. For example, deficits in multisensory integration can result in decreases in speech perception (Irwin, Tornatore, Brancazio, & Whalen, 2011; Smith & Bennetto, 2007), particularly in noisy environments (Foxe et al., 2013). Compromised speech perception may result in missed cues and a potentially chaotic sensory world; thus, it is not surprising that higher ASD severity (as measured by the Autism Diagnostic Observation Schedule; ADOS) is correlated with poorer speech perception (Woynaroski et al., 2013).

Several relevant hypotheses are useful in understanding impairments in multisensory integration within a larger framework of ASD: the Weak Central Coherence hypothesis (Happé & Frith, 2006) and the temporal binding deficit hypothesis (Brock, Brown, Boucher, & Rippon, 2002). The theory of weak central coherence is based on the notion that humans rely heavily on contextual cues to process information such that there is a tendency to perceive the “gestalt” or the “big picture” over individual details. It is proposed that individuals with ASD have a distinct cognitive processing style, in which they “show detail-focused processing in which features are perceived and retained at the expense of global configuration and contextualized meaning” (Happé, 1999, p. 217). The temporal binding hypothesis posits that observed impairments in ASD are a result of reduced neural integration *between* local brain networks and heightened or intact integration *within* networks (Brock et al., 2002). Therefore, neural communication between sensory networks (e.g., visual system and auditory system) may be unreliable. These two theories are useful in considering the apparent lack of multisensory integration observed in ASD. If individuals with ASD perceive sensory units as distinct entities rather than integrated wholes, it is reasonable to speculate that a host of social, communicative, sensory, and behavioural impairments may follow. For example, it has been speculated that characteristic behaviours observed in ASD, such as avoiding looking at faces, may be a compensatory mechanism functioning to limit the amount of perceptual "noise" in their environments (Jones, Quigney, & Huws, 2003; Stevenson, Segers, Ferber, Barense, & Wallace, 2014b).

In addition to the behavioural studies discussed above, self-report (Grandin, 1988), anecdotal (Kanner, 1968), and retrospective video analysis (Baranek, 1999; Osterling & Dawson, 1994) provide clinically meaningful evidence that individuals with ASD process sensory information in atypical, sometimes idiosyncratic ways. Peculiar reactions to sensory information in infants with ASD often predates diagnosis (Adrien et al., 1993). While there is a large body of literature reporting on these sensory processing differences, it is useful to understand how individuals are clinically impacted and whether these impairments follow any discernable pattern. In a large-scale study of children with ASD, 95% of 281 children were reported to have some degree of sensory dysfunction characterized by sensory under-responsiveness across modalities, auditory filtering (e.g., not responding to auditory input), and/or tactile sensitivities (Tomchek & Dunn, 2007). This pattern of sensory processing is supported by the broader literature in this area; however, there is relatively little known about the relationship between these sensory abnormalities and the cognitive operation of multisensory integration.

The Role of Temporal Dynamics in Multisensory Integration

What is at the root of the breakdown in multisensory integration observed in ASD? Timing plays a critical role in the process of multisensory integration, and it is hypothesized that impairments in ASD stem from differences in the temporal perception of multisensory information (Stevenson et al., 2015). For sensory inputs from multiple modalities to be perceived as a unified percept they need to occur within a limited temporal range of each other. The more temporally coincident two inputs are, the more likely they are to be integrated, a probabilistic construct that has been characterized as the *temporal binding window* (TBW; Dixon & Spitz, 1980). The likelihood that two sensory inputs are integrated varies between and within individuals and is influenced by perceptual experiences (Stevenson, Zemtsov, & Wallace, 2012). Individual perceptions of synchrony are influenced by development; as humans mature their TBWs narrow and refine, limiting the amount of information that is perceived as congruent and thus increasing perceptual accuracy (Hillock, Powers, & Wallace, 2011).

Based on research examining the TBWs of individuals with ASD, there is evidence that at least some of the sensory impairments observed in ASD are a function of atypical temporal processing. Contrary to what one may speculate based on the Weak Central Coherence hypothesis, individuals with ASD may be erroneously *over*-binding. In other words, pairing sensory information that should not be bound together. The *flash-beep illusion* is a temporally dependent, low-level multisensory phenomenon that has been employed to explore the TBW in autism (Foss-Feig et al., 2010; Stevenson et al., 2014a). This phenomenon occurs when multiple auditory beeps presented with a single visual flash result in the perception of additional illusory flashes. Interestingly, children with ASD reported the illusion significantly more frequently than typically developing children and had a TBW that was approximately twice the size than that of TD children (Foss-Feig et al., 2010). Importantly, over-binding of sensory inputs that should not be bound results in a decrease in the relevance of binding, and thus reduces the behavioural and perceptual advantages that it incurs. That is, individuals with less precise multisensory temporal perception show a reduction in the behavioural benefits associated with binding (Stevenson, Zemtsov & Wallace, 2012). A wider window of integration in ASD was also reported in a similar study using the flash-beep illusion but with a Temporal Order Judgment (TOJ) task (i.e., report which stimulus occurred first; Kwakye, Foss-Feig, Cascio, Stone, & Wallace, 2011). Findings of an extended TBW in ASD were replicated in a study by Woynaroski and colleagues (2013) using the McGurk effect, suggesting that these findings hold even with more complex, ecologically valid speech stimuli.

Social versus Speech Specific Impairment in ASD

The research presented thus far makes a strong case for atypical multisensory processing in individuals with ASD. However, the degree of impairment and decrease in multisensory temporal precision appears to be linked to stimuli type, in particular, stimuli containing human-related content (e.g., speech, emotion expression). That is, some studies examining audiovisual integration in ASD have reported intact processing of object stimuli, but specific impairments with stimuli containing human faces and voices (Bebko et al., 2006; Mongillo et al., 2008). Given that speech is inherently social (emanates from a person's face) it has been challenging for researchers to determine if impairments in sensory integration are the result of a difficulty processing speech or linguistic information, purely social information, or both. Speech and social stimuli also tend to be more complex and thus are more taxing on processing resources than simple stimuli (e.g., flashes and beeps), which also may account for these differences in processing. A more general impairment in social information is reflective of the social motivation theory of autism, which proposes that individuals with ASD lack an inherent bias to orient to and gain value or pleasure from social stimuli (Chevallier, Kohls, Troiani, Brodkin, &

Schultz, 2012). According to the theory, this initial lack of orienting results in reduced exposure and experience with social information and accounts for the social difficulties observed in ASD.

One of the first studies to examine the role of temporal synchrony in multisensory processing in ASD used a preferential looking paradigm in which participants viewed temporally synchronous and asynchronous presentations of linguistic (woman counting or telling a story) and non-linguistic stimuli (Mousetrap game; Bebko, Weiss, Demark, & Gomez, 2006). The viewing patterns of TD children indicated a preference for temporal synchrony regardless of stimulus content. In contrast, children with ASD preferred synchrony for non-linguistic stimuli, and performed similarly to their TD counterparts, yet demonstrated *random* looking for linguistic stimuli. A follow up study (Lavoie, Hancock & Bebko, in prep), using a four screen design, corroborated previous findings that children with ASD did not display preferential looking for synchrony with linguistic stimuli, whereas TD children did. As in the previous study by Bebko and colleagues (2006), children with ASD and TD did not differ in their preference for synchrony with non-linguistic stimuli. Other studies have found similar results in which individuals with ASD perform significantly lower on audiovisual tasks that involve human faces and speech, but similar to TD children on tasks that used non-human stimuli (e.g., bouncing ball, hammer; Mongillo et al., 2008; Stevenson et al., 2014c). A recent study presented participants with and without ASD with two screens of a person speaking, one of which was synchronous and the other that had a 330ms auditory lead (Grossman, Steinhart, Mitchell, & McIlvane, 2015). In this study, TD but not ASD participants significantly preferred the synchronous screen *even* when ASD participants were explicitly cued to look for the synchronous screen.

The above-described work supports the hypothesis that individuals with ASD have weakened sensitivity to the temporal synchrony of audiovisual speech. However, the impact of the uniquely social quality of speech on audiovisual integration remains unanswered. To date, there is only one study that examined multisensory integration in ASD using social stimuli that did not involve speech. Charbonneau and colleagues (2013) used dynamic, audiovisual depictions of emotions (fear and disgust), which were presented in unimodal and bimodal conditions. They found that TD participants demonstrated significantly greater redundancy gain (faster reaction times) in the multisensory condition compared to participants with ASD (Charbonneau et al., 2013). Furthermore, in a separate task within this study, unimodal conditions were presented with background noise with the signal-to-noise ratio adjusted to reach an 80% accuracy rate. In both visual and auditory conditions, individuals with ASD needed a significantly greater signal-to-noise ratio to reach an 80% accuracy level. Interestingly, this study demonstrated impairment in emotion recognition in ASD that was compromised across unimodal and multimodal conditions and across modalities. This study is one of the first to suggest that social, non-speech conditions are similarly compromised in ASD in terms of multisensory integration. However, the interpretation of these results may be more complicated. Considering that deficits in emotion perception are considered a core feature of ASD, and a potential underlying cause for social and communicative impairments (Bachevalier & Loveland, 2006; Monk et al., 2010; Sigman, Dijamco, Gratier, & Rozga, 2004), the task requirements (choosing an emotion) of the Charbonneau (2013) study may be a potential confound and perhaps not a true indicator of multisensory processing, but rather of emotion processing.

Pupillary Responses as a Psychophysiological Measure

The studies described above used behavioural methods such as perceptual reports or the measure of eye gaze as a dependent variable to understand multisensory processing in ASD. While eye gaze has been a particularly important methodology in this field of study, measures of pupillary responses (i.e. pupil dilation) can be highly informative and collected concurrently. The pupil is the opening in the eye by which light enters, the constriction and dilation of which are controlled by muscles within the iris (Beatty & Lucero-Wagoner, 2000). Response to light is the strongest determinant of pupillary change; however, much smaller fluctuations in pupil size occur as a result of cognitive operations in response to our visual environment and internal experiences (Beatty & Lucero-Wagoner, 2000; Stern, Ray, & Quigley, 2001). Pupillary responses have proven to be a reliable and sensitive indicator of a host of cognitive processes in response to: preference for social stimuli (Fitzgerald, 1968), cognitive difficulty or mental load (Beatty, 1982; Granholm, Asarnow, Sarkin, & Dykes, 1996), orienting of attention (Gabay, Pertzov, & Henik, 2011), emotional arousal (Bradley, Miccoli, Escrig, & Lang, 2008; Stanners, Coulter, Sweet, & Murphy, 1979), and pain (Oka, Chapman, & Jacobson, 2000), to name a few. Furthermore, as a relatively simple, non-invasive technique, pupillary responses have been acknowledged to have great potential in the future of autism research (Martineau et al., 2011).

There has been an effort in the history of examining pupillary responses to understand the role of task complexity (i.e., cognitive load) and physiological arousal, both of which have been shown to be reliable and sensitive indicators of pupillary response (Beatty & Lucero-Wagoner, 2000). The relationship between cognitive load and pupillary responses has been demonstrated across a range of tasks, including arithmetic (Klingner, Tversky, & Hanrahan, 2011), memory (Granholm et al., 1996; Van Gerven, Paas, Van Merriënboer, & Schmidt, 2004), and tasks of perception and attention (Backs & Walrath, 1992; Porter, Troscianko, & Gilchrist, 2007). In particular, researchers have consistently demonstrated that increases in the complexity of speech and language are indicative of greater processing load and can be measured with pupillary response. For example, Just and Carpenter (1993) demonstrated increased pupil dilation in response to reading complex sentences versus simple ones. A more recent study followed a similar line of inquiry by examining pupillary responses to orally presented sentences while manipulating the prosody and visual context (Engelhardt, Ferreira, & Patsenko, 2010). In the auditory condition, participants had greater peak dilations to sentences that were “conflicting” when the prosody of the speaker’s voice did not match the intended meaning of the sentence and were semantically ambiguous. The second study condition included simultaneously presented images (e.g., picture of a person driving) that were either consistent or inconsistent with sentence semantics. Even though sentence comprehension was not directly impacted by the image presented, greater pupil dilation was observed in the inconsistent condition, indicating a greater level of online processing effort when audio and visual information were discordant. This study corroborates a large body of work supporting a strong relationship between pupillary response and task load (i.e., mental effort); however, it offers an added dimension showcasing pupillary response not only to task complexity but also to perceived incongruity (e.g., misaligned prosody interfering with meaning and/or image mismatched with sentence semantics) within the task.

Arousal has also proven to have a consistent effect on pupillary response. Hess (1975) was one of the first to document pupillary dilation in response to images of nudes, which were considered arousing, but also to “pleasing” images, such as an image of a mother and child. Interestingly, Bradley and colleagues (2008) went on to determine that the dilation response was not dependent on emotional valence, and that increased pupil dilation occurs in response to pleasant and unpleasant, but not neutral images. A study using only auditory stimuli found similar results, in that highly arousing positive (e.g., a baby laughing) and negative (e.g., a couple arguing) sounds increased pupil diameter in comparison to neutral (e.g., office noise) stimuli (Partala, Jokiniemi, & Surakka, 2000). While the results of these two studies appear to indicate that pupillary changes occur in response to emotional arousal, independent of valence, others have found greater pupillary responses to unpleasant images compared to pleasant images (Libby, Lacey, & Lacey, 1973).

Furthermore, several studies have indicated that psychopathology or diagnostic conditions which affect emotional and cognitive processing, such as major depressive disorder (Silk, Dahl, Ryan, Forbes, & Axelson, 2007), schizophrenia (Steinhauer & Hakerem, 1992), and ASD (Rubin, 1961), may play a role in differential pupillary responses.

Pupillary Responses in ASD

A relatively small number of studies have examined pupillary responses in ASD. Rubin (1961) was the first to note that children with ASD have a different pattern of dilation and constriction in response to light when compared to typically developed children and adults; however, the sample size in this study was quite small (*ASD group* = 5; *control group* = 4). Since then, a number of studies have used pupillary response as an indicator of autonomic dysfunction in ASD (Anderson, Colombo, & Unruh, 2013) but also as a possible diagnostic bio-marker (Fan, Miles, Takahashi, & Yao, 2009; Martineau et al., 2011). Atypical pupillary responses, such as differences in reflex latency and responses to specific stimuli (e.g., dilation vs. constriction) do indicate that pupillary responses in ASD are distinct from typical neurological performance. For example, Fan and colleagues (2009) found that individuals with ASD exhibited significantly delayed pupillary light reflex (constriction in response to light) and smaller relative constriction compared to TD children and youth. However, there is currently no consensus on findings related to resting (tonic) pupil size in ASD, with reports of pupil sizes that are smaller (Martineau et al., 2011; Rubin, 1961), larger (Anderson & Colombo, 2009; Anderson et al., 2013), or no different from TD controls at baseline (Fan et al., 2009; Nuske, Vivanti, &

Dissanayake, 2014a; Van Engeland, Roelofs, Verbaten, & Slangen, 1991). Fan and colleagues (2009) have suggested that their significant finding of a large between-subject variation in resting pupil size indicates a degree of heterogeneity in ASD, which may play a role in the inconsistencies across studies. The disparities across studies regarding resting pupil size in ASD are somewhat problematic as they limit the generalizability of results and the ability to draw conclusions or make comparisons between studies. Nevertheless, researchers have shown that pupil diameter can be an excellent predictor of group membership and has been successful in correct classification of diagnostic group, with reported rates of 71% (Anderson & Colombo, 2009), 89% (Martineau et al., 2011), and 92 to 100% accuracy (Fan et al., 2009). Thus, the measurement of pupil size has great potential as a non-invasive, early detection method of ASD.

Considering social impairment as a core deficit in ASD, it is not surprising that a number of studies have examined pupillary responses using socially relevant stimuli. Researchers have explored responses to human and animal faces (Anderson, Colombo, & Shaddy, 2006), inverted faces (Falck-Ytter, 2008), and emotional faces to determine if pupillometry is a reasonable method of measuring and understanding the role of social, emotional, and face processing in ASD. In this relatively recent line of inquiry, Anderson and colleagues (2006), were the first to report atypical pupillary constriction in response to children's faces in ASD compared to pupillary dilation in TD children. The same effect was not reported by Martineau and colleagues (2011) who reported no difference in pupillary waveforms in the ASD group in response to objects, avatars, or neutral faces; however, chronologically-age matched controls showed a significant increase in dilation to human faces that was not observed in ASD.

Similarly, there are mixed results in studies that examined the response to faces with emotional expressions. Wagner and colleagues (2013) reported no overall difference in pupil dilation between individuals with and without ASD in response to faces depicting happy and fearful expressions. Sepeta and colleagues (2012) conducted a similar study in which they examined pupillary responses to neutral, happy, fearful, and angry faces in TD and ASD groups; however, they also manipulated the gaze of the face to be either direct or averted. Interestingly, TD children had increased pupil dilation in response to viewing happy faces with a direct versus an indirect gaze, whereas children with ASD did not display pupillary changes sensitive to emotion or gaze direction. Sepeta and colleagues (2012) attribute these findings to impairments in social reward processing in ASD, a system reported to be activated by direct gaze.

A more recent study by Nuske, Vivanti, and Dissanayake (2015) examined the impact of direct and averted gaze with neutral faces on preschoolers with and without ASD. In contrast to Sepeta et al's (2012) findings, Nuske and colleagues found no differences in responding between ASD and TD children, with both groups responding with increased dilation to direct gaze. Another study by the same authors (Nuske, Vivanti, & Dissanayake, 2014b) used video recordings of individuals that were both familiar (i.e., staff at child's daycare) and unfamiliar to the child, in which their expression changed from neutral to fearful in four seconds. Children with ASD had reduced pupillary responses to fearful expressions of unfamiliar but not familiar people. In other words, ASD and TD children showed similar peak dilations in response to familiar people, but only TD children displayed the expected increase in dilation in response to unfamiliar, fearful faces. These findings led the authors to conclude that emotion processing impairments in ASD may be mediated by familiarity and hypothesized that unfamiliar people may be more anxiety provoking for TD children, resulting in increased dilation.

Finally, a negative processing bias in individuals with Asperger's Syndrome (AS), a previously diagnosable category within the ASD umbrella in the DSM-IV (APA, 2000), was reported in a study examining pupillary responses to sentences spoken with neutral, positive, or negative voice intonation (Kuchinke, Schneider, Kotz, & Jacobs, 2011). Using an auditory only condition, this study demonstrated that adult participants with AS had greater pupillary responses (increased dilation) to negatively stated sentences, whereas TD adults had greater responses to positively stated sentences.

The studies discussed here on pupillary response to emotional stimuli in ASD present a somewhat unclear picture. For the most part, researchers report a departure from typical emotional processing in ASD as measured through pupillary changes that are dependent on specific features of the stimuli used, such as emotional expression, familiarity of the face, and direct versus indirect gaze. However, all of the pupillometry studies examining emotion in ASD to date used unimodal stimuli in which either visual or auditory cues were presented in isolation. This presents a potential limitation to the generalizability of these findings. In most social situations, expressions of feeling are accompanied with an emotional tone of voice, emotionally laden speech, and/or non-verbal indicators (e.g., laughing, snickering, sighing, etc.). Emotional stimuli that are multisensory in nature will help to improve the ecological validity of research studies and their relevance to real world scenarios.

In addition to providing insight to important information processing systems in ASD (e.g., emotion processing, face processing, social reward processing), pupillary responses have the potential to provide clinically meaningful information regarding relationships with symptom severity, social behaviour, language, and communication abilities. Anderson et al., (2009, 2013) found that tonic pupil size was correlated with scores on the ADOS (Lord et al., 2000), indicating a possible relationship between autonomic response and severity of autism symptoms. ASD symptoms also appear to be related to strength of emotional reactivity, in this case, pupillary response in reaction to fearful faces (Nuske et al., 2014b). Specifically, greater pupillary response to emotional faces was related to fewer deficits in the areas of communication and play, as measured by the ADOS. Furthermore, Nuske et al (2014b) reported that greater pupillary dilation in response to unfamiliar fearful faces in ASD was related to higher ratings of pro-social behaviour.

From these two studies, it appears that greater pupillary response to social information may be linked to fewer deficits in social communication, a logical link if one considers that greater response and awareness to social stimuli likely translates into improved social skills. In eye-tracking research, gaze behaviour in typically developing infants has been found to be predictive of intelligence later in life (Colombo, 1995; Kavšek, 2004; Sigman, Cohen, & Beckwith, 1997); however, there are mixed findings regarding the role of IQ and pupillary response. In two studies using socially-driven tasks different results were reported; in one there was no relationship between pupillary response and IQ in children with ASD (Sepeta et al., 2012), and in the other there was a significant relationship between increased pupillary response to a joint attention task and non-verbal IQ in TD children (Erstenyuk, Swanson, & Siller, 2014). Specifically, Erstenyuk et al. (2014), presented two joint attention conditions, a 'congruent' condition, in which a model directed her gaze at a target, and an 'incongruent' condition in which the model's gaze was directed in a location different from the target. Interestingly, significant associations were related to the incongruent condition: 1) greater pupil dilation was related to lower non-verbal intelligence, and 2) greater pupil dilation was related to fewer subclinical ASD symptoms (as measured by the Social Responsiveness Scale; Constantino & Gruber, 2002). On one hand, these findings seem to suggest that lower cognitive functioning is associated with an increase in processing load, which fits with the resource allocation interpretation of pupillometry (Granholm et al., 1996). On the other hand, greater social abilities were also associated with an increase in resource allocation, which also fits with previous interpretations with higher social skills being associated with greater responses to social stimuli (Nuske et al., 2014b) and the social reward processing hypothesis (Sepeta et al., 2012). Continued and rigorous investigation is necessary to better understand the nuanced contributions of cognitive processing and emotional arousal on pupillary responses and how they apply to individuals with ASD.

Current Study

The rationale for the proposed study is based on the premise that pupil responses are linked to cognitive processing and arousal. Specifically, the current study examines pupillary responses in children with ASD and typically developing (TD) children as an indicator of cognitive processes involved in the multisensory integration of social and non-social information. This study introduces a number of novel elements to the study of pupillary responses in ASD. First, this study will be the first to examine pupil responses with dynamic, multisensory stimuli rather than unisensory stimuli (e.g., only images, only an audio track), increasing the ecological validity of stimuli and the generalizability of the study. Second, this study will examine multisensory processing in ASD using pupil responses to temporally synchronous and asynchronous audiovisual stimuli. Manipulation of temporal synchrony and concurrent measurement of pupillary responses will allow for a novel indicator of multisensory integration as well as the associated cognitive load of multisensory perception. The design of the current study will include several stimulus types that will answer a number of unique research questions. Stimuli will be grouped broadly into social versus non-social, with the social grouping including the following three types: social-linguistic, social non-linguistic, and social-emotional (further explained in the Methods section). The intended result is to parse out the effects of language and emotion from purely social stimuli, while maintaining multisensory properties, to understand better the contribution of each of these elements to core impairments in ASD. Furthermore, pupillary data gathered in this study will help clarify whether the previously-found differences in gaze behaviour between social and non-social stimuli typically observed in ASD were a result of processing load or arousal (i.e., social information is more difficult to process, therefore, it is avoided). Finally, it is also a major goal of this study to understand the relationships between pupillary responses to social and non-social stimuli and real world factors such as social skills, ASD symptom severity, and sensory processing.

Research Objectives and Hypotheses

For a brief overview of research objectives, see Table 1. Overarching research objectives are four-fold:

Objective 1: Characterize pupillary responses to social and non-social information in typical development and ASD

1. Pupillary responses to social and non-social information will differ overall and there will be different responses between TD children and children with ASD.
    a) TD participants – It is expected that typically developing participants will have greater pupil dilation in response to social versus non-social information, due to it being inherently more complex and potentially arousing than non-social stimuli.
    b) ASD participants – For the ASD group, there are two possible outcomes predicted: 1) There will no difference between pupillary responses for social and non-social stimuli due to social information not being perceived as important or engaging, or 2) It is possible that social information may be even more arousing

and cognitively taxing to children with ASD than for TD children, due to a novelty/inexperience factor and greater pupillary responses will be observed in this condition.

2. Within social stimuli, there will be differences in pupillary responses to linguistic, non-linguistic, and emotional conditions.
    a) TD Participants – It is predicted that pupillary responses will be observed from largest to smallest in the order of most to least socially meaningful information: 1) emotional, 2) linguistic, and 3) non-linguistic.
    b) ASD Participants – Since emotional stimuli have evolutionary significance, it is expected that individuals with ASD will show the greatest response to emotional stimuli, but that responses to linguistic and non-linguistic stimuli will be similar. All responses will be smaller (change from baseline) in comparison to TD participants.

Objective 2: Characterize pupillary responses to asynchronous and synchronous audiovisual stimuli

3. Pupil size will vary in response to asynchronous versus synchronous audiovisual stimuli with different patterns of responding based on diagnostic group.
    a) TD Participants – Based on previous studies which documented greater pupillary response to incongruent conditions (Engelhardt et al., 2010), it is expected that asynchronous conditions will be more cognitively difficult to process and greater pupil dilation will be observed compared to synchronous presentations.
    b) ASD Participants – Based on previous research indicating that individuals with ASD are less sensitive to temporal asynchrony (Bebko et al., 2006), it is predicted

that there will be no overall difference between synchronous and asynchronous conditions in ASD.

4. The effect of asynchrony will be dependent on stimulus type.
    a) TD Participants – It is expected that the effect of asynchrony as measured by increased pupil dilation will be greatest for social stimuli compared to non-social stimuli, due to a greater degree of importance in accurately perceiving social information.
    b) ASD Participants – It is expected that there will be greater sensitivity to temporal asynchrony in the non-social, non-linguistic condition (indexed by greater change in pupil dilation between synchronous and asynchronous conditions) compared to the social conditions. This expectation is based on previous results (Bebko et al., 2006) in which ASD participants displayed a preference for non-social synchronous information, but not for social stimuli.

Objective 3: Determine whether pupillary responses can accurately distinguish ASD from typical development

5. Baseline measurement of pupil size during viewing of a grey screen will be recorded to determine if it can predict diagnostic group membership.
    a) The inclusion of a baseline trial will serve the purpose of making a baseline comparison between ASD and TD groups. Due to previous accounts of smaller (Martineau et al., 2011; Rubin, 1961), larger (Anderson & Colombo, 2009; Anderson et al., 2013), and equal resting pupil size in ASD (Fan et al., 2009; Nuske et al., 2014a; Van Engeland et al., 1991), this question is exploratory in nature and no specific hypothesis is made.

6. Pupillary responses during viewing of experimental stimuli will predict diagnostic group membership.
    a) It is predicted that the hypothesized patterns of responding to experimental stimuli (see objective 1 and 2) will allow for above chance prediction of group membership.

Objective 4: Understand the relationship between pupillary responses and measures of ASD symptoms and social factors

7. Pupillary responses to social or non-social stimuli will be associated with ASD symptom severity including social impairment and restricted and repetitive behaviours.
    a) TD Participants – Based on Erstenyuk et al's (2014) findings, it is predicted that there will be a negative association between scores of social impairment and pupil dilation in response to social stimuli. That is, larger pupil dilations to social stimuli will be associated with lower scores of social impairment on the social responsiveness scale (SRS-2; Constantino & Gruber, 2012).
    b) ASD Participants – Based on Nuske et al's (2014b) findings, it is predicted that there will be a negative association between pupil size in response to social stimuli and measures of ASD severity: the social responsiveness scale (SRS-2; Constantino & Gruber, 2012), the autism diagnostic observation schedule (ADOS-2; Lord, C., Rutter, M., DiLavore, P. C., Risi, S., Gotham, K., & Bishop, 2012), and the repetitive behaviours questionnaire (Leekam et al., 2007).
8. Pupillary responses to asynchronous stimuli will be associated with ASD symptom severity including social impairment and restricted and repetitive behaviours for the ASD group only.

a) TD Participants – Significant relationships between response to asynchrony and ASD symptoms severity are not expected for the TD group.

b) ASD Participants – It is predicted that greater pupillary response to asynchrony (compared to synchronous stimuli) will be associated with lower scores on measures of ASD symptoms (social impairment and restricted and repetitive behaviours).

9. Pupillary responses to asynchronous stimuli will be associated with sensory processing difficulties in ASD participants only.

   a) TD Participants – This is an exploratory research question; however, since TD children do not normally experience sensory processing sensitivities it is not expected that there will be a great degree of variability in participant scores on the sensory processing measure (SP-2; Dunn, 2014) and; therefore, will not have a significant association with pupillary responses.

   b) ASD Participants – It is expected that there will be a relationship between participants who have high sensory sensitivity (as measured by the "Sensor" domain of the SP-2) and greater pupillary responses to asynchronous stimuli. Individuals scoring higher on the "Registration/Bystander" domain of the SP-2, indicating a low level of sensory registration, are expected to have a negative association with pupillary response to asynchronous stimuli.

Table 1
Hypotheses and Predicted Outcomes for Conditions and Diagnostic Group

Hypothesis	Condition or Measures	Predicted response in TD	Predicted response in ASD
#1	Social vs. Non-social	Greater dilation to social	Two possible outcomes: 1) no difference or 2) greater dilation to social
#2	Social-Emotional vs. Social-Linguistic vs. Social Non-linguistic	Dilations will be greatest for Social-Emotional, followed by Social-Linguistic, and Social-Non Linguistic	Dilations will be greatest for Social-Emotional, but no difference between Social Linguistic and Social Non-linguistic
#3	Synchronous vs. Asynchronous	Greater dilation to asynchrony	No difference between asynchrony and synchrony
#4	Synchronous vs. Asynchronous Social vs. Non-social	Greater dilation to asynchronous social stimuli	Greater dilation to asynchronous non-social stimuli
#5	Baseline (grey screen)	Exploratory analyses to determine whether diagnostic group membership is predicted by pupil size	
#6	All Experimental Conditions	Above predicted patterns will predict diagnostic group membership	
#7	ASD symptomatology and pupillary response to Social stimuli	Negative association – higher ASD symptomatology will be associated with smaller dilations for both groups	
#8	ASD symptomatology and pupillary response to Asynchronous stimuli	No relationship	Negative association – lower ASD symptomatology will be associated with greater pupil dilations
#9	Sensory processing and pupillary response to Asynchronous stimuli	No relationship	Positive association - higher sensory processing scores (i.e., greater sensitivity) will be associated with increased dilation to asynchrony

Methods

Participants

A total of 74 participants were tested for this study between August 2014 and January 2015. Depending on location tested, participants were recruited through word of mouth, community organizations (e.g., church groups; autism organizations), research partnerships, and online advertisements. Forty participants had ASD and were classified into the clinical group; ASD participants were tested in Cincinnati, Ohio, USA (*n* = 19) and in Toronto, Ontario, Canada (*n* = 21). Membership in the ASD group was initially determined by parent report of an ASD diagnosis. Presence of ASD was verified during testing through administration of the Autism Diagnostic Observation Schedule (ADOS-2; Lord, Rutter, DiLavore, Risi, Gotham, & Bishop,

2012) and review of a diagnostic report from a health-care professional (e.g., psychiatrist, psychological, family doctor), which parents were asked to provide.

The TD group (*n* = 34) was tested in Brampton, Ontario, Canada (*n* = 16), Toronto, Ontario, Canada (*n* = 14), and Cincinnati, Ohio, USA (*n* = 4). Three participants (2 TD, 1 ASD) were excluded from further analyses due to significant loss of eye-tracking data, with the final number of participants totaling 71. See Table 2 for descriptive statistics regarding sex, chronological age, mental age, and IQ for each group. As is typical for this clinical population, there were more males (76.9%) in the ASD group, than females, whereas the TD group was comprised of more females (71.9%) than males; the difference in sex distribution between groups was significant ($X(1) = 16.907$, $p < .001$). To ensure that differences in response to stimuli were not dependent on sex, a Repeated Measures 2 (Sex) x 4 (Stimuli) ANOVA was performed. Responses to stimuli did not vary as a function of sex as evidenced by a non-significant main effect of Sex ($F(1, 69) = 1.070$, $p = .305$, $\eta^2_{partial} = .015$) as well as a non-significant interaction between Sex and ($F(2.185, 150.787) = .061$, $p = .952$, $\eta^2_{partial} = .001$). In terms of chronological age, the groups had comparable means, standard deviations, and ranges and did not differ significantly from one another ($t\ (69) = -.123$, $p = .903$). To determine whether differences in intelligence were present between groups, mental age was calculated using Full-Scale IQ Scores from two subtests on the WASI (see Measures section) and was not significantly different between groups ($t\ (69) = -1.269$, $p = .209$). Participants with ASD had significantly lower FSIQ scores on the WASI ($t\ (69) = -2.059$, $p = .043$) than TD participants; however, when comparing verbal and non-verbal subscales this difference was significant for the Vocabulary subtest ($t\ (69) = -3.020$, $p = .004$), but not for Matrix Reasoning ($t\ (69) = -1.099$, $p = .276$).

Table 2.
Participant Demographic Information

Total N = 71	**ASD (Total N = 39)**	**TD (Total N = 32)**
Sex	M = 30 (76.9%); F = 9 (23.1%)	M = 9 (28.1%); F = 23 (71.9%)
	M (SD)	
Chronological Age (CA)	12.3 (3.2) yrs range = 6.8 – 20.0 yrs	12.4 (3.0) yrs range = 6.4 – 18.7 yrs
Full Scale IQ (FSIQ – 2)	94.0 (22.2) range = 45 – 145	102.8 (10.6) range = 86 – 121
Mental Age (CA*FSIQ)÷100	11.5 (4.2) yrs range = 4.9 – 20.3	12.7 (3.2) yrs range = 5.5 – 19.6
Non-Verbal T-Score (Matrix Reasoning)	47.3 (13.2) range = 20 – 71	50.3 (8.7) range = 36 – 77
Verbal T-Score (Vocabulary)	46.0 (14.1) range = 20 – 70	54.6 (8.7) range = 39 – 72

Strict measures were taken to ensure that testing conditions were kept constant across locations. The same testing equipment was used at each location and the same experimenters were involved in each testing session. Furthermore, a strict protocol was followed in delivering instructions to participants.

Exclusionary criteria. Participants were required to have normal or correct-to-normal vision and hearing. Participants were expected to have at least a 2-year-old verbal ability in English and expected to have the cognitive capacity to understand and complete task requirements. Testing procedures were explained to parents to determine whether a child would be able to participate and IQ was verified with formal testing. Participants' parents were asked that children not take any medication on the day of testing, including over the counter medications (e.g., cold medicine). Furthermore, participants were asked to refrain from consuming caffeine (e.g., coffee, soda, chocolate) on the day of testing. In cases where children were medicated or consumed caffeine on the day of testing, pertinent information was recorded (e.g., type of medication).

Measures

Wechsler Abbreviated Scale of Intelligence – Second Edition (WASI-II; Wechsler, 2011). Participants in both groups were administered the WASI-II, a reliable measure of intelligence designed for individuals aged 6 – 90. This abbreviated measure of IQ has a two-subscale option, FSIQ-2, that can be administered within 15 minutes. To increase efficiency and decrease participant fatigue, one verbal task and one non-verbal task were administered to obtain a full-scale IQ based on two subtests. A *verbal reasoning* score was derived from a vocabulary task in which participants defined the meanings of words and a *perceptual reasoning* score was derived from the matrix reasoning task, in which participant completes a visual pattern. The WASI-II is strongly linked to and parallels items on the more comprehensive Wechsler tests (e.g., WISC-IV, WAIS-IV) and is suggested by the authors to provide a reasonable estimate of intelligence. The WASI-II has been modeled after the WISC-IV and WAIS-IV in both internal structure and test content. The WASI-II correlates highly with similar instruments (WASI-I, WISC-IV, and WAIS-IV), ranging from .71 to .92. The WASI-II also has strong reliability in a sample of children aged 6-16 years. Using the split-half method reliability coefficients for subtest scores ranged from good (.87) to excellent (.91) and the average reliability coefficient for the FSIQ-2 was .93. The test-retest reliability for the FSIQ-2 for children 6 to 16 was .89 and the adult sample, age 17 – 90, had a correlation of .94.

Child Sensory Profile – Second Edition (Dunn, 2014). The Child Sensory Profile was designed for caregivers of children between the age of 3 and 14 years. In this study, participants above 14 years of age also completed the Adolescent/Adult Sensory Profile (Brown & Dunn, 2002) if they were deemed cognitively able; however, all participants had a caregiver report completed for consistency. The Sensory Profile includes 86 items designed to evaluate a child's sensory processing patterns in the context of their everyday lives (e.g., home, community) and takes between 5 to 20 minutes to complete. Each item presents parents with a statement (e.g., *My child . . . ignores sounds, including my voice*) to which they must indicate the degree of their response: Almost Always (90% or more of the time), Frequently (75% of the time), Half of the Time, Occasionally (25% of the time), Almost Never (10% or less of the time), or Does Not Apply (the behaviour has never been observed or does not apply to my child). It provides scores for responses to different sensory systems: Auditory, Visual, Touch, Movement, Body Position, and Oral, which allow for modality specific analysis or identification of difficulties. It also provides scores within the following behavioural domains: Attention, Conduct, and Social-Emotional that provide an indication of how sensory processing may be contributing or interfering with a child's participation in their home, social lives, and community. The Sensory Profile-2 provides scores indicating specific patterns of processing, divided across four quadrants: registration, seeking, sensitivity, and avoiding. Finally, the resulting score profile allows for the categorization of how the individual scored in relation to their same-aged peers using the following categories: much less than others, less than others, just like the majority of others, more than others, and much more than others. The Sensory Profile 2 was normed on 1791 children, including 774 children with disabilities such as ASD, ADHD, and Down Syndrome. The SP-2 fares well in terms of reliability, with test-retest reliability values from .83 to .97 and inter-rater reliability between .70 and .80.

Social Responsiveness Scale – Second Edition (SRS-2; Constantino & Gruber, 2012). The School-Age Form of the SRS-2 contains 65 items and is considered an objective measure of symptoms associated with ASD. The SRS-2 School-Age Form can be completed in 15 – 20 minutes by the caregiver of a child or youth and is designed for children and youth ages

4 to 18. Items are provided as statements to which caregivers respond on a Likert-scale the degree to which the statement characterizes their child: 1) not true, 2) sometimes true, 3) often true, and 4) almost always true. The SRS-2 was designed to measure the severity of social impairment characteristic of those on the autism spectrum. Summed scores indicate whether a child or youth falls “within normal limits,” in the “mild range” (clinically significant deficiencies in social behaviour that have a mild interference with everyday interactions), in the “moderate range” (clinical significance, substantial interference), or in the “severe range” (clinical significance, severe interference). Items on the SRS-2 fall into five “treatment” subscales (termed so for their use in designing and evaluating treatment programs): Social Awareness (the ability to pick up on social cues), Social Cognition (interpreting social cues), Social Communication (expressive social communication), Social Motivation (extent of motivation for social-interpersonal behaviour), and Restricted Interests and Repetitive Behaviour. The School-Age Form was standardized with a large sample of 1, 014 school aged children with diversity representative of the U.S. population. The authors of the SRS-2 report strong reliability with internal consistency between alpha values of .92 to .95. Inter-rater agreement collected across parent and teacher ratings indicate correlations of .77 and .61, respectively (Bruni, 2014). The scale has good concurrent validity and is strongly correlated with similar measures such as the Social Communication Questionnaire (Rutter, Bailey, & Lord, 2003), the Children’s Communication Checklist (Bishop, 1998), the Social and Communication Disorders Checklist (Skuse, Mandy, & Scourfield, 2005), and the Childhood Autism Rating Scale (Schopler, Reichler, DeVellis, & Daly, 1980). The authors of the SRS-2 report that 93% of children who score above their indicated cut-point (70) for an ASD go on to receive a diagnosis in a comprehensive assessment, demonstrating good predictive validity.

Repetitive Behaviours Questionnaire – Second Edition (RBQ-2; Leekam et al., 2007). The RBQ-2 is completed by caregivers and is 20 items in length, which was shortened from the original 33-item version (RBQ). Items fall into four categories: unusual sensory interests, repetitive motor movements, rigidity/adherence to routine and preoccupations with restricted patterns of interest. Items are posed in the form of a question (e.g., *Does your child . . . repetitively fiddle with toys or other items?*) to which parents are asked to indicate a rating of frequency, 1 = never or rarely, 2 = one or more times daily, 3 = 15 or more times daily (or at least once an hour), 4 = 30 or more times daily (or twice an hour) *or* with a rating of severity, 1 = rarely or never, 2 = mild or occasional, 3 = marked or notable.

The RBQ-2 was developed from two previously existing measures: The Repetitive Behaviours Interview (RBI; Turner, 1996) and the Diagnostic Interview for Social and Communication Disorders (DISCO; Wing, Leekam, Libby, Gould, & Larcombe, 2002). Both the original RBQ and the DISCO have been used in a number of research studies and demonstrate good inter-rater reliability (Wing et al., 2002). The RBQ-2 was normed on 679 children under the age of 3 (Leekam et al., 2007) and in another study with 15 month olds (Arnott et al., 2010) in England. The internal consistency within these samples was high (Cronbach's $\alpha = .85$) indicating that the RBQ-2 is a useful instrument for measuring repetitive behaviours in children. The RBQ and RBQ-2 has also now been researched in samples with ASD and children and youth up to 17 years of age (Honey, McConachie, Turner, & Rodgers, 2012; Lidstone et al., 2014; South, Ozonoff, & McMahon, 2005; Zandt, Prior, & Kyrios, 2007) and proved to be a useful and reliable tool in the measurement of restricted and repetitive behaviours both in ASD and typical populations.

Autism Spectrum Quotient – Child Version (Auyeung, Baron-Cohen, Wheelwright, & Allison, 2008)

The Autism Quotient – Child Version is designed for children aged four to eleven years old but was used with all participants regardless of age for consistency and comparison purposes. The AQ was completed by the participant's caregiver and assesses five areas typically associated with autistic traits: social skills, attention switching, attention to detail, communication, and imagination. Each scale is represented by 10 items, and each item is rated on a 4 point Likert scale, with higher scores corresponding with increased ASD symptoms. The AQ has the ability to discriminate between individuals with ASD and typically developing individuals with a high degree of sensitivity (95%) and specificity (95%). The AQ has high internal consistency (Cronbach's $\alpha = .97$) and test-retest reliability ($r = .85$).

Autism Diagnostic Observation Scale – Second Edition (ADOS-2; Lord, et al., 2012). The ADOS-2 is a semi-structured observational measure used in the diagnosis of ASD at different developmental levels and chronological ages. The ADOS-2 has five modules (T – toddler, 1, 2, 3, and 4) each of which contains a schedule of activities and tasks designed for use with children or adults at a particular developmental and language level. Tasks are designed to elicit behaviours in order to assess communication, social interaction, play, imaginative use of materials, and level of restricted and repetitive behaviours. Participant behaviours and responses to tasks are coded within categories relevant to a diagnosis of ASD: *social affect (SA)*, including communication and reciprocal social interaction, and *restricted and repetitive behaviours (RRB)*. The ADOS-2 was administered by a trained clinician and took approximately 40 – 60 minutes to administer; only modules 1 through 4 were used in this study due to the age range of our participants. A clinically trained member of the research team was also present to assist in the readying of materials and for training purposes. Each administration was video recorded for training and scoring verification. The inclusion of the ADOS-2 allowed for verification of an ASD diagnosis in the clinical sample.

The ADOS-2 is the revised and updated version of the ADOS, which is considered the "gold standard" in the observational assessment of ASD (Kanne, Randolph, & Farmer, 2008). The development of the ADOS-2 included an extended validation (1,574 children) and replication sample (1,282 children), and possesses similarly strong psychometric properties as the original ADOS. The internal consistency for modules 1 through 3 was good for the social affect domains with Cronbach's α values between .87 to .92; however, moderate values were reported for the restricted and repetitive behaviours domains (.51-.66). Module 4 was not revised and thus retains the psychometric properties of the original ADOS, with α values exceeding .75 for the communication domain, .85 for the social interaction domain, and .47 for the RRB domain. In terms of test-retest reliability, reports indicate correlations from .68 to .92 from a sample of 75 participants with an average of 10 months between testing. For inter-rater reliability, raters had between 92-98% agreement on diagnostic classifications for Modules 1 through 3. Finally, content and construct validity has been evaluated through factor analyses, which identified the Social Affect domain and the RRB domain as making significant independent contributions to the prediction of diagnosis; however, the overall total score produced the highest predictive value of diagnosis. The predictive value of the ADOS-2 has been maintained and/or improved with the second edition, with sensitivity ranging from 60%-95% and specificity ranging from 75%-100% (McCrimmon & Rostad, 2013).

Stimuli

Baseline stimuli and inter-stimuli slides. A series of fixation crosses were presented to participants for two minutes at the start of the experiment for the purpose of obtaining a baseline reading of pupil diameter from both eyes (Anderson et al., 2013). Baseline images consisted of a grey background and a coloured cross; to retain interest in the baseline stimulus, every 10 seconds the colour of the cross changed. Twelve images were presented and luminance was standardized across the baseline images and with each frame of all experimental stimuli using Matlab (Natick, MA; procedure described below). Inter-stimuli slides were presented between experimental trials as a black fixation cross on a grey background for an interval of three seconds.

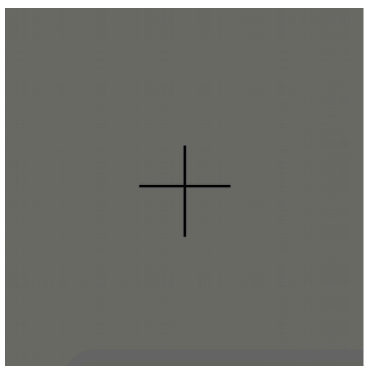

Figure 1. Example of an inter-stimulus slide. Presented for a duration of 3 seconds between experimental stimuli.

Experimental stimuli. Each trial consisted of an audiovisual presentation of a video clip for duration of five seconds. Stimuli were divided into several categories. First, stimuli were either social or non-social; social trials were defined by the presence of a person's face in the video whereas the non-social clips were predominantly of moving objects. There were two types of non-social clips: 1) a ball moving through a series of coloured slides, stairs, and levers from the game, Mousetrap (Milton Bradley) and 2) a close-up shot of a person's fingers playing a short melody on piano keys. The social clips had three types: linguistic, non-linguistic, and emotional and the same two actresses were used for the creation of all three social sub-categories. The linguistic conditions were clips of a woman telling a simple story of which there were several versions. The non-linguistic conditions were clips of a female making a series of varied sounds using her mouth (e.g., kissing sounds, popping sounds) with neutral affect. The emotional condition consisted of each actress expressing either happiness or sadness by making facial expressions, facial movements, and noises consistent with these emotions (e.g., laughing, giggling, snorting). Each stimulus type was presented in three modes: synchronous, asynchronous audio-leading, and asynchronous visual-leading. Synchronous presentations were synched in audiovisual output, while in the asynchronous conditions, either the audio or the video led by 1 second. This length (1 second) was chosen as an adequate amount of time in which asynchrony could be readily detected by young children with ASD and typical development. This judgment was based on work by Stevenson et al. (2014c), who examined the temporal binding windows for children with and without ASD of a similar age range to this study (6 – 18 years). They presented parametrically varied stimulus onset asynchronies at 50ms intervals with social-linguistic stimuli up to +/- 400ms, and found binding window widths well below the maximum possibility, ~600ms in ASD and ~425ms in typically developing children and youth (Stevenson et al., 2014c). Furthermore, both audio-leading and visual-leading presentations of asynchrony were included to prevent the occurrence of "temporal adaptation" or a decrease in sensitivity to temporal asynchrony with continued exposure in a particular direction (e.g., only audio-leading stimuli; Harrar & Harris, 2008; Navarra et al., 2005). This same phenomenon is observed following greater exposure to asynchronous versus synchronous stimuli (Segers & Bebko, 2012).

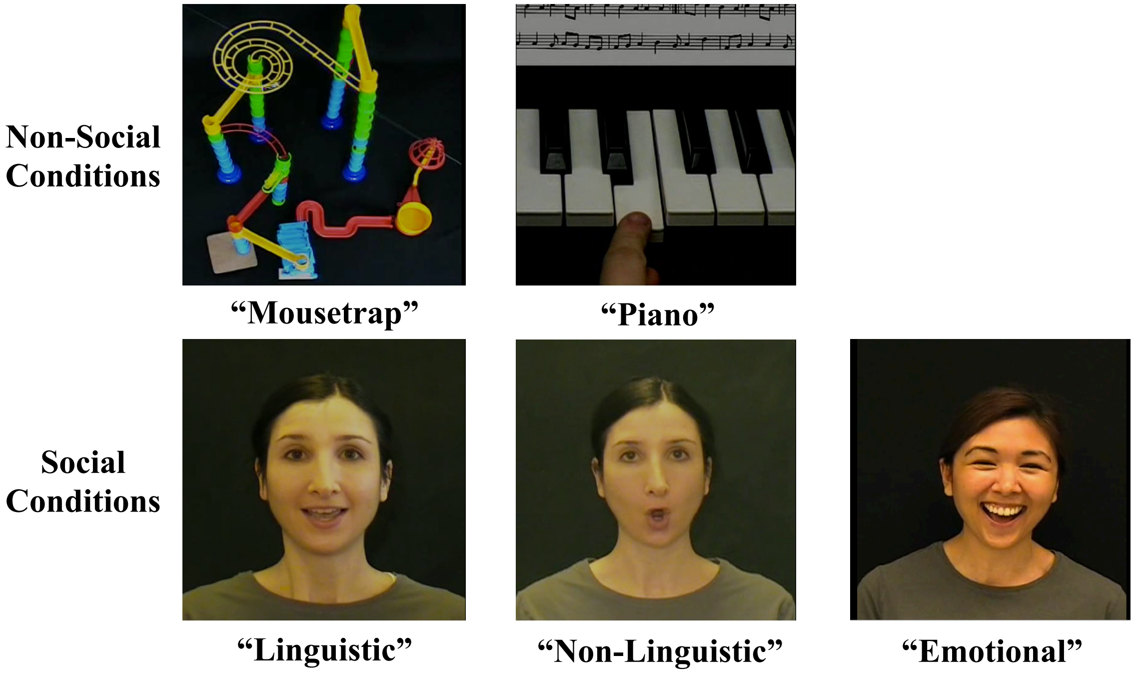

Figure 2. Example still images of experimental video clips. Video clips were presented for a duration of 5 seconds.

Clips were filmed using a Sony handheld camera, edited using Final Cut Pro, and converted to DIVX format as required for presentation in E-prime. The auditory volume for each trial was tested with a handheld audiometer and adjusted using Final Cut Pro. Each clip was tested to ensure that: 1) the peak volume did not exceed 60 dB and, 2) the average volume of the clip fell between 55 – 60 dBs. The luminance across all clips was standardized by: 1) separating video files from audio files, 2) standardizing the luminance for each individual frame within a video clip using MatLab, and 3) re-creating the video from the image sequences and adding the audio to the clip. Stimulus presentation order was pseudo-randomized such that each version of each condition was preceded and followed by every other version of each condition only once. Four different versions of each trial type were created; this was achieved by using multiple actresses and by using separate segments from a longer clip. Each separate clip was presented once at each temporal offset: synchronous, audio-leading, and visual leading. Therefore, across versions, each trial type was presented twice per block, which resulted in 30 trials per block and a total of 120 trials (see Table 3 for a breakdown of trials). After each block, there was a short break to allow participants to rest their eyes or adjust their position. The break between the second and third block, indicating the halfway point of the experiment, was one minute in length and the other two breaks were 10 seconds long. Altogether, including calibration procedures, breaks, the baseline trial, and experimental trials, the eye-tracking portion of this study took approximately 30 minutes to complete.

Table 3.
Stimulus Map: Sample (unrandomized) Block Showing All Conditions and Versions

Condition	**Description**	**Synchronization**	**Actor/Version**
Social Linguistic	Stories	Synchronous	Actor 1
Social Non-Linguistic	Non-speech sounds	Synchronous	Actor 1
Social-Emotional - Happy	Laughing	Synchronous	Actor 1
Social-Emotional - Sad	Crying	Synchronous	Actor 1
Non-Social Non-Linguistic	Mousetrap	Synchronous	Version 1 of 2
Social Linguistic	Stories	Audio-Leading	Actor 1
Social Non-Linguistic	Non-speech sounds	Audio-Leading	Actor 1
Social-Emotional - Happy	Laughing	Audio-Leading	Actor 1
Social-Emotional - Sad	Crying	Audio-Leading	Actor 1
Non-Social Non-Linguistic	Mousetrap	Audio-Leading	Version 1 of 2
Social Linguistic	Stories	Visual-Leading	Actor 1
Social Non-Linguistic	Non-speech sounds	Visual-Leading	Actor 1
Social-Emotional - Happy	Laughing	Visual-Leading	Actor 1
Social-Emotional - Sad	Crying	Visual-Leading	Actor 1
Non-Social Non-Linguistic	Mousetrap	Visual-Leading	Version 1 of 2
Social Linguistic	Stories	Synchronous	Actor 2
Social Non-Linguistic	Non-speech sounds	Synchronous	Actor 2
Social-Emotional - Happy	Laughing	Synchronous	Actor 2
Social-Emotional - Sad	Crying	Synchronous	Actor 2
*Non-Social Non-Linguistic	Piano	Synchronous	Version 1 of 2
Social Linguistic	Stories	Audio-Leading	Actor 2
Social Non-Linguistic	Non-speech sounds	Audio-Leading	Actor 2
Social-Emotional - Happy	Laughing	Audio-Leading	Actor 2
Social-Emotional - Sad	Crying	Audio-Leading	Actor 2
*Non-Social Non-Linguistic	Piano	Audio-Leading	Version 1 of 2
Social Linguistic	Stories	Visual-Leading	Actor 2
Social Non-Linguistic	Non-speech sounds	Visual-Leading	Actor 2
Social-Emotional - Happy	Laughing	Visual-Leading	Actor 2
Social-Emotional - Sad	Crying	Visual-Leading	Actor 2
*Non-Social Non-Linguistic	Piano	Visual-Leading	Version 1 of 2

* indicates condition was not included in final analyses.

Procedure

All protocols related to this study were approved by the Office of Research Ethics at York University Human Participants Review Sub-Committee (certificate number #2014 – 160).

Apparatus. Stimuli were presented to participants through a desktop computer that was connected to a 27 by 16-inch monitor set at a resolution of 1280 x 720 pixels. Stimuli were presented using E-Prime presentation software, E-Studio, and eye movements were recorded with a Tobii X60 eye-tracker at a sampling rate of 60Hz. Participants were seated in front of the eye-tracker with their eye-line level with the middle of the screen approximately 60 cm from the screen. A booster seat was used to raise shorter participants and books were used to raise the height of the screen for taller participants. Once positioned, a calibration procedure was performed to ensure accuracy in eye movement recordings. A second, smaller monitor was positioned with the screen out of participant eyesight to monitor the status of the eye-tracker throughout the testing session. To ensure standardization of volume and sound, participants wore noise-isolating headphones throughout the experimental task.

General procedure. Upon arrival participants and their parents were greeted and the consent process was initiated. A research assistant remained with parents to complete informed consent and provide them with the parent-report questionnaires (Autism Quotient, Sensory Profile - 2, Social Responsiveness Scale - 2, and the Repetitive Behaviours Questionnaire - 2). Verbal or written assent was obtained from participants prior to commencing the experimental task. All participants first completed the experimental task, which was followed by the intelligence assessment (WASI-II) and the autism assessment (ADOS-2; only participants in the ASD group). Participants were provided with breaks, snacks, and beverages as needed throughout. Upon completion, participants and their parents were thanked, provided with a $10 gift certificate to a bookstore, and reimbursed for parking or travel expenses. The entire duration of the study was approximately two hours in length for typically developing participants and three hours in length for participants with ASD (with the inclusion of the ADOS - 2 making the difference between groups).

Experimental procedure. Participants were presented with a familiarization procedure and nine practice trials (3 synchronous, 3 audio-leading, 3 visual-leading, randomized) that were five seconds in length prior to starting the experimental task (these examples were not presented in the experimental portion of the study). During the familiarization phase, participants were presented with a cartoon clip approximately 10 seconds in length in which the audio and video were synchronized. Their task during this clip was simply to observe the screen. Next, participants were informed that they would observe a second clip, which was similar to the one they just observed, with one major difference. Participants were cued to spot the difference between the two clips. The second clip was presented with the audio preceding the visual by 1 second. The majority of participants were able to recognize that the second clip was out of synch, but were not required to indicate whether it was audio-leading or visual-leading. A small number of participants were not able to indicate their understanding of the differences in synchrony between the two clips.

Once the familiarization phase was complete, participants were ready to begin the experimental task. Prior to the presentation of videos, participants viewed a series of coloured fixation crosses for 2 minutes, for the purpose of obtaining a baseline pupillary reading. Participants were instructed to remain calm and still and to continue watching the crosses. An instruction screen appeared prior to presentation of stimuli and participants were also verbally reminded of the task.

Conditions

This study was designed with five conditions, each of which had four different versions presented to participants: 1) Social-Linguistic, 2) Social Non-Linguistic, 3) Social-Emotional Happy, 4) Social-Emotional Sad, and 5) Non-Social Non-Linguistic. In the social conditions, different versions were created by varying the actor and the timing of the video clip resulting in unique content for each version. In the Non-Social Non-Linguistic condition, versions were created by changing the content, in this case, Mousetrap or Piano. The original intent was to treat Mousetrap and Piano as versions within the same Non- Social Non- Linguistic category. Initial analyses revealed that for both groups, responses differed greatly between Mousetrap and Piano trials and indicated that they should not be treated as equivalent, or as counterparts within one category. Subsequent review of the literature indicates that music is known to elicit differential pupillary responses (Gingras, Marin, Puig-Waldmüller, & Fitch, 2015) and brain activation patterns (Koelsch, 2014; Panksepp & Bernatzky, 2002), suggesting that it is processed differently from other types of non-social information. Since the purpose of this study was to focus on comparing social processing to non-social processing, and not musical processing, the piano condition was excluded from all subsequent analyses. Furthermore, for simplicity of analyses, the two emotional conditions Social-Emotional Happy and Social-Emotional Sad were combined to create one Social-Emotional condition.

Data Processing

Areas of Interest (AOIs) were delineated in Tobii Studio to capture pupil data that were recorded while the participant was engaged with relevant aspects of the stimuli, rather than focusing their gaze in the periphery of the screen. Specifically, a restricted AOI was created including only the area of the video in which movement and essential information was captured for each respective stimulus type (i.e., Face, Mousetrap). For example, for social stimuli the AOI included only the area of the face, whereas for non-social stimuli the AOI captured the area of the screen where the ball was sliding down a tube for Mousetrap. The total area of the AOI was the same across stimulus type, but the placement of the AOI on the screen varied depending on the stimuli. Pupillary data was exported from Tobii Studio software in Microsoft Excel spreadsheets and further processed in MatLab before analysis in Statistical Package for the Social Sciences (SPSS). Data was inspected for artifacts such as blinks, loss of tracking, head movements and subsequently corrected using linear interpolation. Useable data consisted of pupil traces at least 500ms in length in which artifacts did not make-up more than 20% of the pupil trace (as per guidelines put forth by Anderson et al., 2006). Data were used in instances where data were captured from both eyes, which were averaged together. The arithmetic mean of each individual's pupil size was calculated in response to each of the stimulus conditions and subtracted from the mean pupil size of the preceding inter-stimulus trial, which served as a baseline for each trial. Baseline data was captured from the last 1000ms of each inter-stimulus trial directly preceding stimulus onset; if no data was present during that timespan (e.g., the participant closed their eyes or looked away from the screen), the first useable data point during stimulus presentation was set as the baseline for that trial. To ensure that pupillary data was captured during the most informative time points, mean pupil values between the 1st to 4th second of each stimulus presentation were used in data analyses. Based on inspection of pupillary waveforms, pupillary response to stimuli were negligible in the 1st second of stimulus onset and was not included in the analysis. This assessment is consistent with similar research in which pupil dilation peaked roughly 1000ms following stimulus onset or a cognitive demand (Erstenyuk et al., 2014; van der Meer et al., 2010).

Missing Data

A missing value analysis was completed to explore possible patterns of missing data and determine an appropriate approach to dealing with missing values. Only the dependent variable of mean pupillary response for each condition was examined for missing data. Of the fifteen conditions, ten had some proportion of missing values, ranging from 1.4 – 7% of values (see Table 4). Nine participants (12.7%; 8 ASD, 1 TD) out of the entire sample had some degree of missing data, which overall represented only 2.2% of all values. To prevent loss of statistical power that would result from exclusion of nine participants, further analysis was completed to determine if data were missing randomly. Little's MCAR test of "missingness" indicated that data were not MCAR (missing completely at random; $X^2(100, N = 71) = 145.847$, $p = .002$). However, the data satisfied the criterion of MAR (missing at random), in which systematic "missingness" was correlated with other study variables, in this case, number of trial presentations (Baraldi & Enders, 2010). Due to the fact that the Piano condition was excluded from further analyses, the Non-Social Non-Linguistic condition had only half as many presentations as other conditions, resulting in fewer opportunities to gather solid pupil traces that satisfied study requirements (described above). Therefore, study variables and not participant characteristics, resulted in data that were MAR. Further analysis of missing data patterns revealed no significant patterns of missingness. In the case that data are MAR, multiple imputation is considered the most sophisticated approach to dealing with missing data that produces unbiased parameter estimates (Baraldi & Enders, 2010). Therefore, multiple imputation was employed to address cases of missing data using the following variables as predictors: all available pupil data, group membership (TD or ASD), sex, mental age, total score on the Sensory Profile, and total score on the Autism Quotient – Child Questionnaire. From these predictor variables, ten imputed data sets were produced and a new "pooled" data set was comprised of an average of all ten data sets.

Table 4.
Missing Data Analysis

	Missing	
Condition	**N**	**%**
Non-Social Non Linguistic _Sync	5	7
Non-Social Non Linguistic _VA	4	5.6
Non-Social Non Linguistic _AV	4	5.6
Social Linguistic_Sync	3	4.2
Social Emotional Happy_ VA	2	2.8
Social Emotional Sad_ AV	1	1.4
Social Emotional Sad_ Sync	1	1.4
Social Non-Linguistic_Sync	1	1.4
Social Linguistic_VA	1	1.4

Assumptions of General Linear Model

To ensure that all assumptions of the General Linear Model were met, variables were examined for normality. A normality assessment entailed visual inspection of Normal Q-Q plots, observation of guidelines for values of skewness and kurtosis z-scores (above +/- 1.96) and the Shapiro-Wilk normality test (see Appendix A). The majority of variables (11/15) were normally distributed, and while several variables exceeded cut-off values, variables were deemed to be approximately normally distributed. Other assumptions were also met including the assumption of homogeneity of variances, which was measured by the Levene Statistic (see Appendix A). Of the fifteen variables, only one variable (Social Linguistic_VA) had a p-value <.05 indicating significantly different variances. Finally, observations were considered to be independent and the dependent variable (pupil diameter) was measured on an interval scale.

Results

Omnibus Repeated Measures ANOVA Test

To test the effect of the entire model, a three way, 2 (Group) x 4 (Stimuli) x 3 (Synchrony) Repeated Measures Analysis of Variance was performed. For this test Stimuli was reduced to four categories in which the two emotional conditions Happy and Sad were combined to produce one Social-Emotional condition; thus the conditions tested included: Social Linguistic, Social Non-Linguistic, Social-Emotional, and Non-Social Non-Linguistic. Mauchly's test of sphericity indicated that the assumption of sphericity was violated for Stimuli ($\chi^2(5)$ = 32.597, p = .000), and the Synchrony by Stimuli interaction ($\chi^2(20)$ = 68.966, p =.000), but not for Synchrony alone ($\chi^2(2)$ = 3.512, p =.173). Therefore, degrees of freedom were corrected using Greenehouse-Geisser estimates of sphericity for Stimuli (ε = .739) and the Synchrony by Stimuli interaction (ε = .710).

Individuals with ASD had significantly smaller pupillary changes from baseline compared to the TD group, as indicated by a main effect of group, $F(1, 69) = 5.496$, p = .022, $\eta^2_{partial}$ = .074. There was a significant main effect of Stimuli ($F(2.216, 152.932) = 4.177$, p = .014, $\eta^2_{partial}$ = .057), and a main effect of Synchrony that was approaching significance ($F(1.904, 131.386) = 3.021$, p = .055, $\eta^2_{partial}$ = .042). Neither the Synchrony by Group ($F(1.904, 131.386) = .213$, p = .798, $\eta^2_{partial}$ = .003), nor the Stimuli by Group ($F(2.216, 152.932) = 1.821$, p = .161, $\eta^2_{partial}$ = .026) two-way interactions were significant. However, there was a significant two-way interaction between Synchrony and Stimuli ($F(4.261, 294.029) = 2.508$, p = .039, $\eta^2_{partial}$ = .035). The three-way interaction of Synchrony by Stimuli by Group was non-significant ($F(4.261, 294.029) = .283$, p = .899, $\eta^2_{partial}$ = .004). *A Priori* determined hypotheses were explored using post hoc comparisons, correcting for multiple comparisons with the Sidak correction.

Objective 1 Results

The first study objective was to characterize pupillary responses to social and non-social information between typically developing children and children with ASD. These results are presented graphically in Figure 3.

Hypothesis 1: Pupillary responses to social and non-social information.

To address the first hypothesis, pairwise comparisons between each group and stimulus type were performed. Comparisons revealed that TD children had larger dilations than ASD children for Social-Linguistic ($t(69) = 2.705$; $p = .009$, $d = 0.653$), Social Non-Linguistic ($t(69) = 2.869$; $p = .005$, $d = 0.681$), and Social-Emotional ($t(69) = 2.035$; $p = .046$, $d = 0.490$) stimuli. There were no significant group differences, however, for the Non-Social Non-Linguistic condition ($t(69) = .892$; $p = .376$, $d = 0.214$).

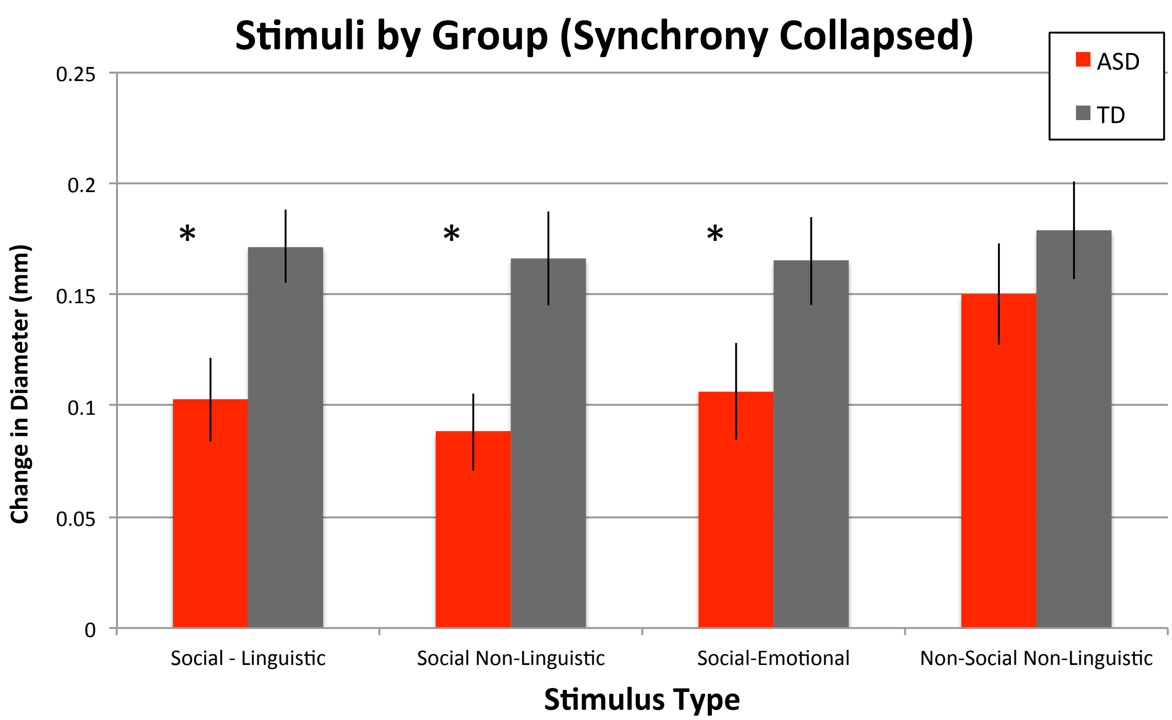

Figure 3. Change in pupil diameter for stimulus type. * Indicates a p < .05 difference between ASD and TD.

For the purpose of understanding how responses differed between Social and Non-Social conditions, within-group comparisons were also conducted. In the ASD group, pupil dilation to the Non-Social Non-Linguistic condition was significantly larger than for each of the social conditions: Social-Linguistic ($t(38) = 2.373$; $p = .023$, $d = 0.386$), Social Non-Linguistic ($t(38) = 3.250$; $p = .002$, $d = 0.537$), and Social-Emotional ($t(38) = 2.325$; $p = .025$, $d = 0.374$). Comparisons between social conditions were all non-significant. In the TD group, pairwise comparisons did not reveal any significant differences between any of the stimulus types (*p's > .400)*.

Hypothesis 2: Pupillary responses within social conditions.

To address Hypothesis 2, a Repeated Measures 2 (Group) x 3 (Stimuli) ANOVA including only social conditions (presented in synchrony) was performed. This analysis revealed a significant main effect of Stimuli ($F(2, 138) = 5.308$, $p = .006$, $\eta^2_{partial} = .071$) and a main effect of group ($F(1, 69) = 6.092$, $p = .016$, $\eta^2_{partial} = .081$). The interaction between Stimuli and Group was non-significant ($F(2, 138) = .123$, $p = .885$, $\eta^2_{partial} = .002$). These results are depicted in Figure 4. Between-group comparisons revealing significant differences between groups for each stimulus type: Social-Linguistic ($t(69) = 2.096$; $p = .040$, $d = 0.497$), Social Non-Linguistic ($t(69) = 2.201$; $p = .031$, $d = 0.525$), and Social-Emotional ($t(69) = 2.176$; $p = .033$, $d = 0.521$). Within-group comparisons for the ASD group revealed that the difference between the Social Non-Linguistic and Social-Emotional was approaching significance ($t(38) = 2.013$; $p = .051$, $d = 0.326$), with non-significant relationships between the other conditions. In the TD group, pupillary response to the Social Linguistic ($t(31) = 2.066$; $p = .047$, $d = 0.366$) and Social Non-Linguistic condition ($t(31) = 2.514$; $p = .017$, $d = 0.446$) were significantly smaller than for the

Social-Emotional condition, but not significantly different from each other ($t(31) = .278$; $p = .783$, $d = 0.049$).

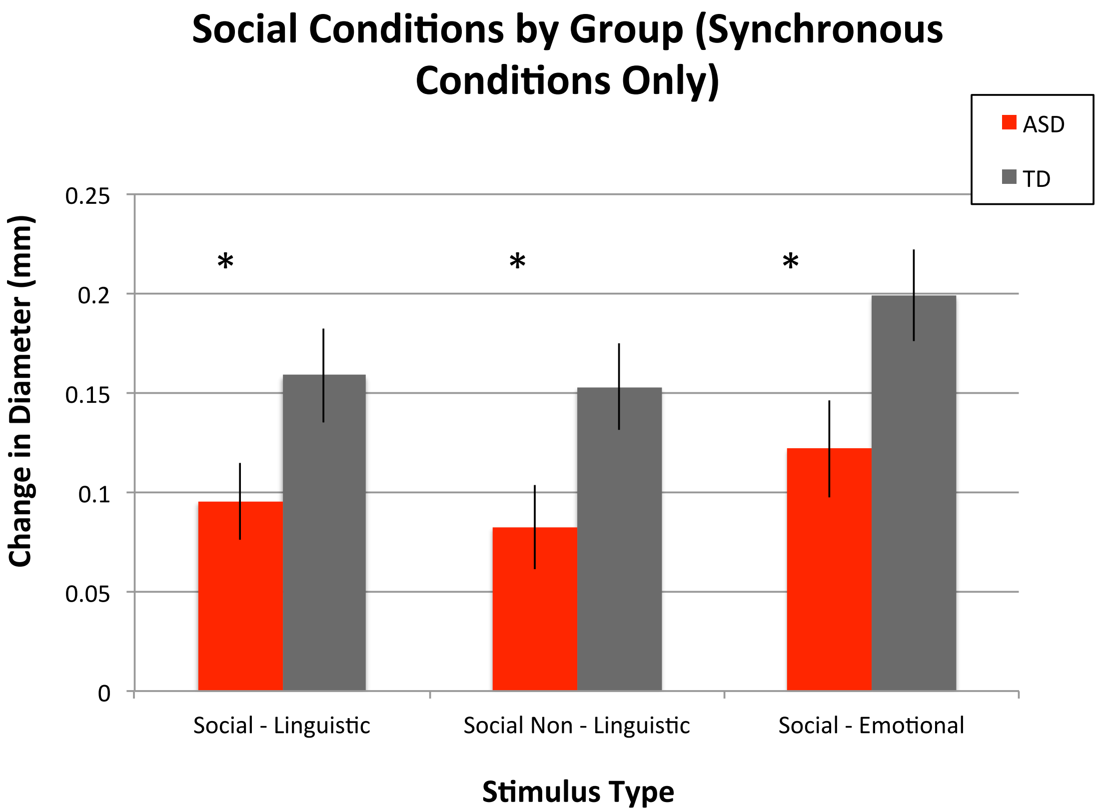

Figure 4. Change in pupil diameter within social conditions. * Indicates a $p < .05$ difference between ASD and TD.

Objective 2 Results

The second objective of this study was to characterize children's pupillary responses to asynchronous and synchronous audiovisual stimuli. Further, the goal was to determine whether asynchronous audio-visual presentations had a differential effect on pupillary response that was dependent on stimulus type.

Hypotheses 3 & 4: Pupillary responses to asynchrony.

Based on the results from the omnibus ANOVA (see above), which indicated a non-significant interaction between group and synchrony, all participants were combined (TD and

ASD) for temporal processing analyses to understand the role of asynchrony and stimulus type on pupillary response. Thus, a 4 (Stimuli) x 3 (Synchrony) Repeated Measures ANOVA was conducted. Results revealed a significant main effect of Stimuli ($F(2.185, 152.930) = 4.714$, $p = .008$, $\eta^2_{partial} = .063$) and a main effect of Synchrony approaching significance ($F(2, 140) = .213$, $p = .057$, $\eta^2_{partial} = .040$). There was also a significant Stimuli by Synchrony interaction ($F(4.273, 299.131) = 2.487$, $p = .040$, $\eta^2_{partial} = .034$). These results are presented in Figure 5.

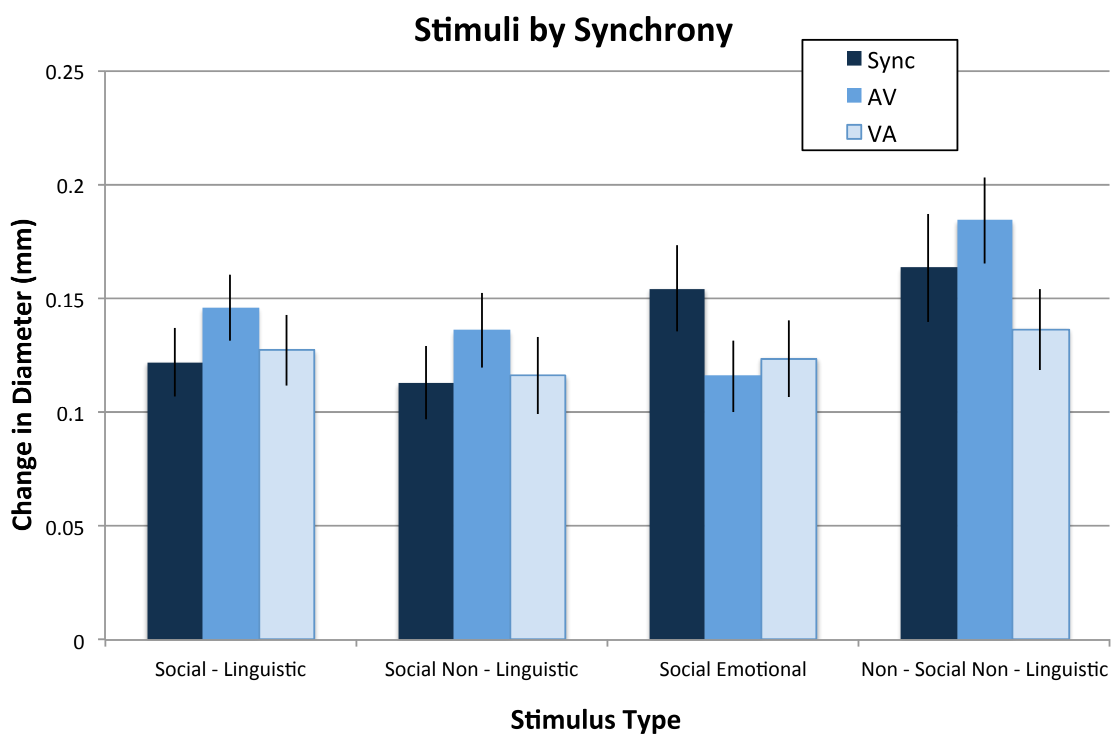

Figure 5. Change in pupil diameter across synchrony and stimuli. Note that ASD and TD participants are combined into a single group.

Within-stimulus pairwise comparisons were conducted to understand relationships to synchrony for each particular stimulus type. For both Social-Linguistic and Social Non-Linguistic conditions there were no significant differences among variations in synchrony. In the Social-Emotional condition there were significant differences between Synchrony and Audio-Leading ($t(70) = 3.617$; $p = .001$, $d = 0.456$), and Synchrony and Visual-Leading ($t(70) = 2.767$;

$p = .007$, $d = 0.336$). Differences between Audio-Leading and Visual-Leading in the Social-Emotional condition were non-significant ($t(70) = .724$; $p = .472$, $d = 0.086$). In the Non-Social Non-Linguistic condition, there was a significant difference between Audio-Leading and Visual-Leading presentations ($t(70) = 2.685$; $p = .009$, $d = 0.319$), but not between other presentations.

Pupillary Time Course Analysis.

Pupil time course analyses were included as an additional exploratory analysis of pupillary response to experimental conditions as a function of time. Figures 6 – 9 depict mean pupillary change from baseline for each stimulus type for group and synchrony. For each condition, paired sample *t*-tests for each 100ms interval were performed to determine group differences within synchronous and asynchronous (AV and VA conditions collapsed) presentations. Time course analyses offer a graphical representation of the results of the previously discussed ANOVAs with the added variable of time. In the Social-Linguistic condition (Figure 6), TD individuals showed an earlier and greater dilation response than individuals with ASD. While both groups appeared to peak at close to the same time following stimulus onset (between 2.2 – 2.4s), the ASD group had a smaller and more gradual response. Further, we can observe that in the TD group, there was a slightly greater response to asynchrony, while the opposite pattern was observed in ASD. Figure 6 also depicts, along the x-axis, the duration of time points at which group differences were significant for synchronous and asynchronous presentations, both occurring between 1 – 3 seconds. A similar pattern was observed in the Social Non-Linguistic condition (Figure 7), but with a larger discrepancy between synchrony and asynchrony for the TD group. In this condition, there were no significant group differences in synchronous presentations; however, typically developing children had much greater dilations to asynchrony than children with ASD from roughly 1 – 3.5s post stimulus onset.

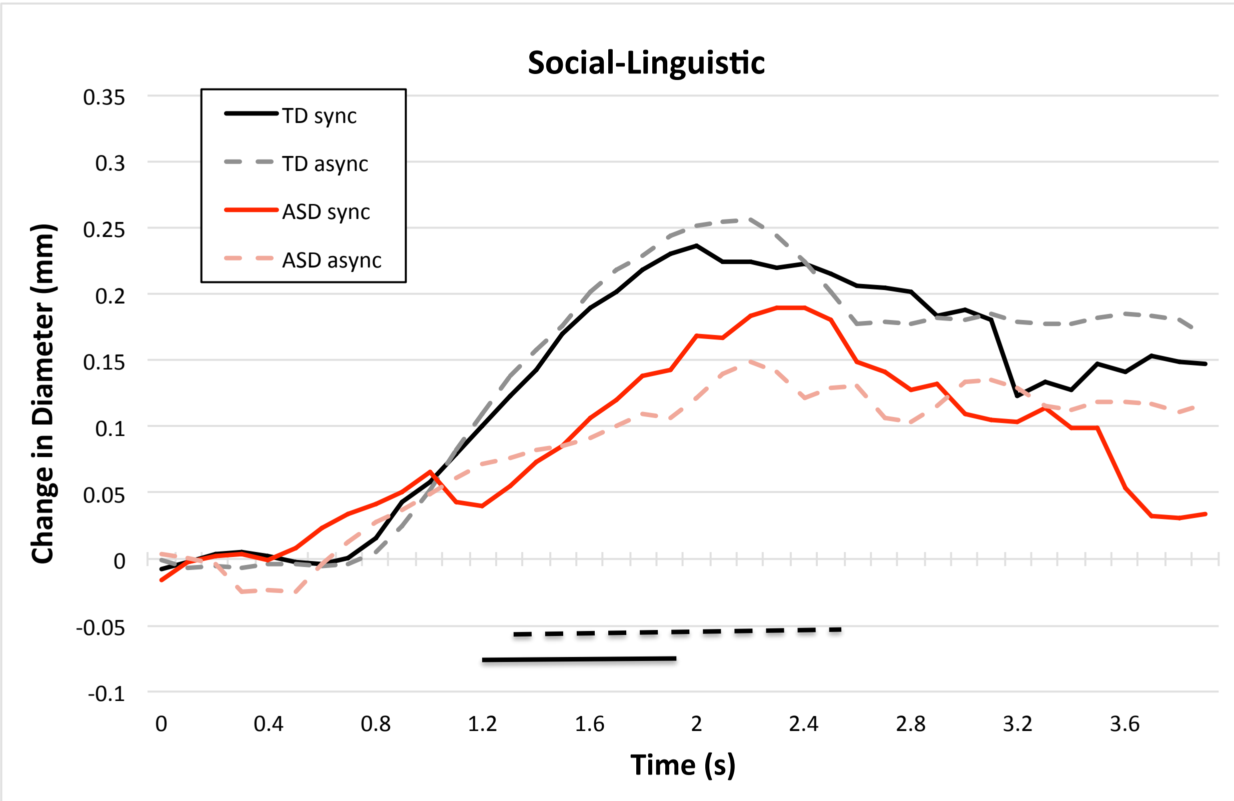

Figure 6. Mean pupillary waveform depicting change in dilation over time for TD and ASD groups. Dashed and solid lines above the x-axis indicate significant group differences (paired t-test, $p < .001$) during that period. The solid line indicates the difference between synchronous conditions (1.2 – 1.9s) and the dashed line indicates differences between asynchronous conditions (1.3 – 2.5s).

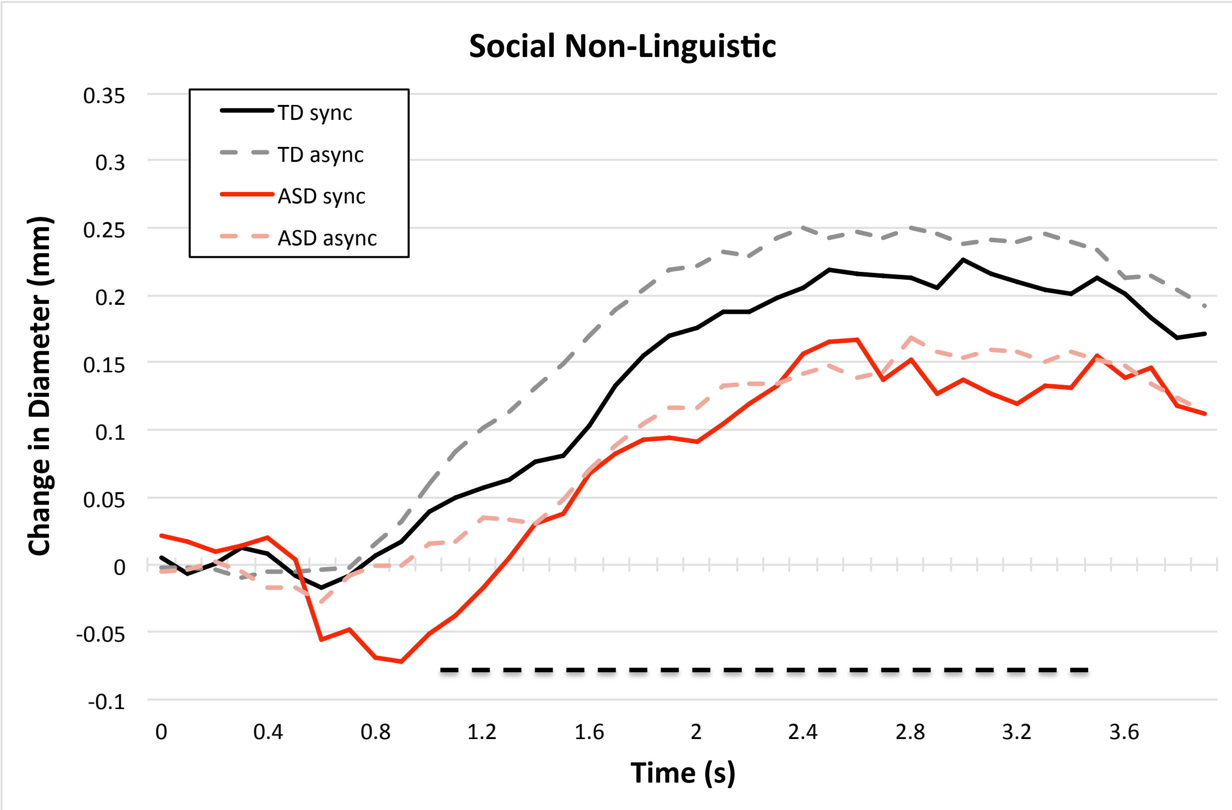

Figure 7. Mean pupillary waveform depicting change in dilation over time for TD and ASD groups. Dashed line above the x-axis indicates significant group differences (paired t-test, $p < .001$) for the asynchronous condition from 1 – 3.5s. There were no significant group differences between synchronous conditions.

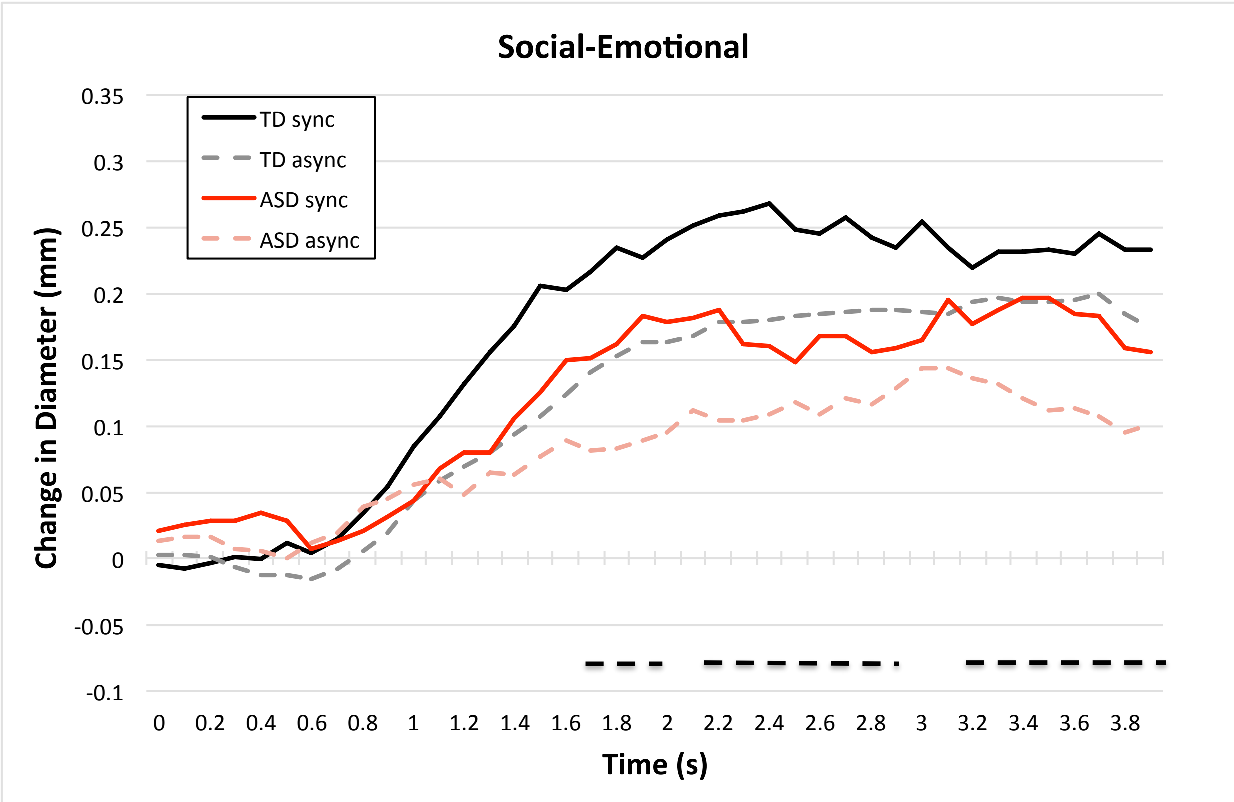

Figure 8. Mean pupillary waveform depicting change in dilation over time for TD and ASD groups. Dashed line above the x-axis indicates significant group differences (paired t-test, $p < .001$) for the asynchronous condition for the indicated periods (1.7 – 2s; 2.2 – 2.9s; 3.2 – 3.9s). There were no significant group differences between synchronous conditions.

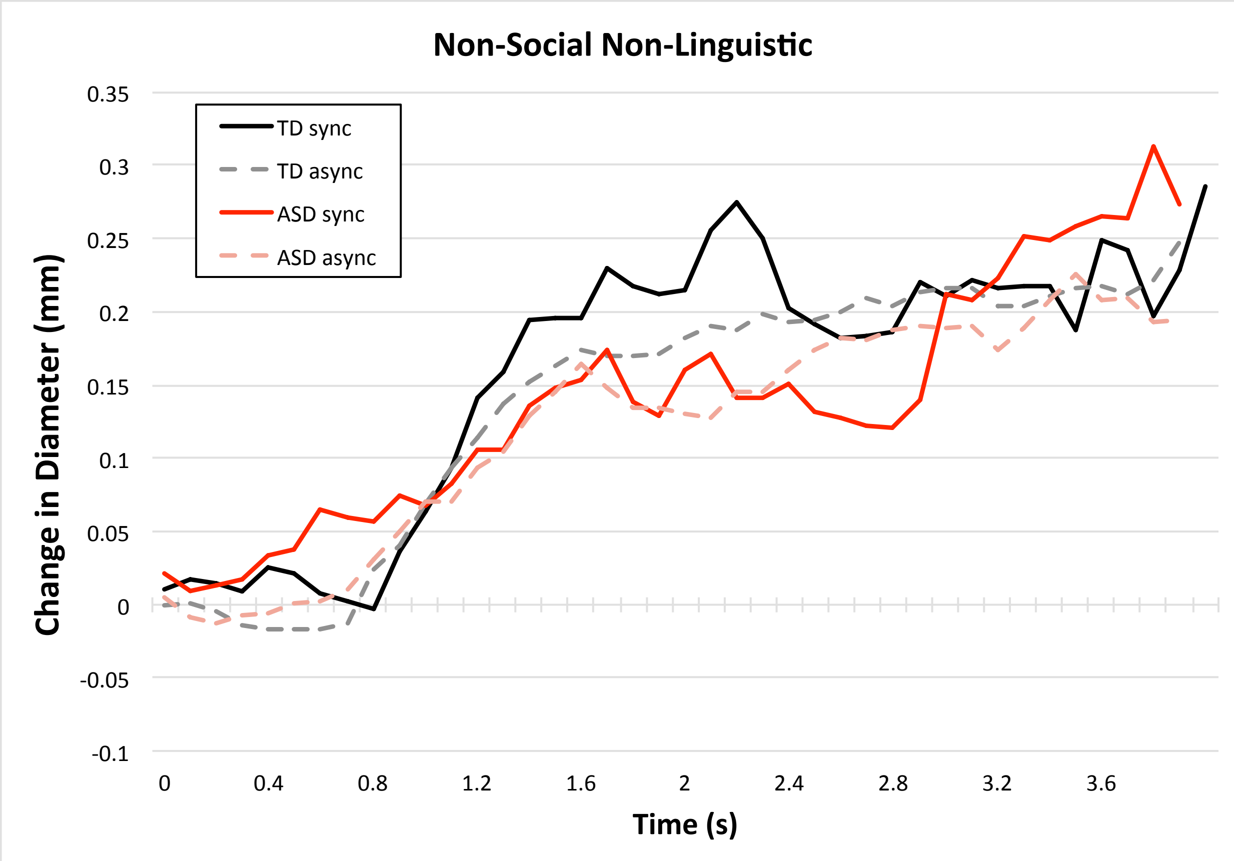

Figure 9. Mean pupillary waveform depicting change in dilation over time for TD and ASD groups. There were no significant group differences between synchronous or asynchronous conditions.

The Social-Emotional condition is depicted in Figure 8 and mirrors previously reported results from the ANOVA testing the effect of synchrony (Hypothesis 4). Pupillary responses for the Social-Emotional condition differ from the pattern observed for the two other social conditions (Social-Linguistic and Social Non-Linguistic). Specifically, for both the TD and ASD groups, pupillary responses were greater for synchronous presentations than for asynchrony. Finally, in the Non-Social Non-Linguistic condition (depicted in Figure 9) there were no significant group differences for either synchronous or asynchronous presentations. There was a similar response in both groups in which pupils tended to dilate in a gradual and increasing slope that did not return to a downward trajectory within the time frame analysed.

Objective 3 Results

The third objective was to determine whether pupillary responses would meaningfully predict group membership (ASD or TD) significantly above chance.

Hypothesis 5: Baseline measurement as predictor of group membership.

At the beginning of the experiment, participants viewed a fixation cross which changed colour every 10 seconds (to retain interest) for a two-minute period. The length of the baseline trial was to ensure an extended period in which to obtain stable pupillary traces from all participants. An independent *t*-test indicated that individuals with ASD (M = 4.074, SD = .540) did not differ significantly in their baseline pupil size from the TD (M = 4.047, SD = .414) sample in this study ($t(69) = .231$, $p = .818$, $d = 0.056$).

Inter-stimulus trials were used as a baseline measure when calculating pupillary change in response to experimental conditions. These trials were 3 seconds in length, with pupillary traces from the last 1 second of the inter-stimulus trial used in comparison to experimental trials to allow for adequate return to resting pupil state. Mean pupil size across all inter-stimulus baseline trials indicated that individuals with ASD (M = 4.297, SD = .636) had slightly larger pupil size than TD individuals (M = 4.070, SD = .423), but this difference was only approaching significance ($t(69) = -1.468$, $p = .073$, $d = 0.420$). Considering that there were no differences between groups, pupillary response to baseline (pre-experiment, inter-stimulus) was not considered a useful predictor of group membership.

Hypothesis 6: Responses to stimuli as predictor of group membership.

Results from the above tested hypotheses and consideration of theory-driven questions dictated the order in which variables were entered into a hierarchical logistic regression to predict group membership (see Table 5 for complete information). A logistic regression was chosen over other possible methods (i.e., linear discriminant analysis) as it is considered the most flexible and robust method for prediction of a dichotomous outcome variable (Pohar, Blas, & Turk, 2004). Due to established between-group differences on three of the four stimulus types, and no significant main effect or interaction of synchrony, variables were collapsed across synchrony type prior to being entered into the model. First, the Non-Social Non-Linguistic condition was entered as the first step into the model to determine whether pupillary responses to non-social information had any ability to predict group membership. Pupillary response to the Non-Social Non-Linguistic condition did not reliably predict group membership, indicated by insignificant parameter and model statistics at Step 1 (χ^2 (1) = .802, p = .370). Next, the Social Non-Linguistic condition was entered into the model to determine the impact of a social condition without the presence of language or emotional content. The contribution of *socialness* alone, resulted in a model that was significantly more predictive than with the constant alone, or with Non-Social Non-Linguistic alone (χ^2 (2) = 8.789, p = .012). Nagelkerke's R^2 test of effect size increased from .015 to .156 with the addition of the Social Non-Linguistic condition, greatly increasing the amount of variance accounted for by the overall model. In Step 3, the Social-Linguistic condition was added to the model to determine the effect of language on the predictive power of group membership. While the overall model remained significant, the Social Non-Linguistic condition lost its significance as an individual predictor. The same pattern was observed in Step 4, with the addition of the Social-Emotional condition, with a significant overall model (χ^2 (4) = 9.760, p = .045), and none of the predictors being significantly predictive above and beyond the others.

Table 5.
Hierarchical Logistic Regression Analysis of Group Membership

Model Steps	**Predictor**	**B**	**SE B**	**Wald's χ^2**	***df***	***p***	**e^B (Odds Ratio)**
Step 1 Predictors:	*Non-Social Non-Linguistic*	.162	.181	.802	1	.370	1.176
				χ^2	***df***	***p***	**Nagelkerke R^2**
Step 1 Evaluation				.811	1	.368	.015
Step 2 Predictors:	Non-Social Non-Linguistic	-.227	.236	.924	1	.336	.797
	Social Non-Linguistic	.757	.284	7.096	1	.008	2.131
				χ^2	***df***	***p***	**Nagelkerke R^2**
Step 2 Evaluation				8.789	2	.012	.156
Step 3 Predictors:	Non-Social Non-Linguistic	-.265	.242	1.193	1	.275	.767
	Social Non-Linguistic	.531	.388	1.869	1	.172	1.701
	Social-Linguistic	.336	.401	.701	1	.402	1.399
Step 3 Evaluation				**χ^2**	***df***	***p***	**Nagelkerke R^2**
				9.502	3	.023	.168
Step 4 Predictors:	Non-Social Non-Linguistic	-.223	.256	.758	1	.384	.800
	Social Non-Linguistic	.615	.425	2.092	1	.148	1.849
	Social-Linguistic	.433	.449	.933	1	.334	1.542
	Social-Emotional	-.219	.433	.256	1	.613	.803
				χ^2	***df***	***p***	**Nagelkerke R^2**
Step 4 Evaluation (Final Model)				9.760	4	.045	.172

* Hosmer & Lemeshow's goodness-of-fit tests were insignificant ($p > .05$) at each step of the model.

The above pattern of results indicates that the final model was a significantly better fit to the data than the null model. Further, an insignificant *p*-value for the Hosmer and Lemeshow test ($\chi^2(8)= 8.991$, $p = .343$) indicates that the final model is a good fit to the observed data. Interestingly, following the inclusion of the Social-Linguistic condition, none of the variables appeared to contribute significantly to the model individually. This type of effect might be due to issues with multi-collinearity, a high degree of correlation between predictors. Point-biserial correlational analyses indicate that, indeed, the three "social" predictor variables were highly related to one another (each relationship $r \geq .814$, $p < .01$). Collinearity statistics were further assessed and indicated acceptable values for Tolerance (greater than .1; Menard, 1995) and Variance Inflation Factor (VIF; less than 10; Myers, 1990). However, given large discrepancies between Eigenvalues it is highly possible that multi-collinearity is affecting the results of the regression (Field, 2005). This interpretation appears to explain the results of the logistic regression in that "socialness" was the critical element contributing to the significance of the model. When additional social variables were added (in Step 3 and 4), all the social variables accounted for the same variance and were not significantly predictive within the presence of the other social variables. To test whether the order of entry into the hierarchical regression significantly affected this outcome and interpretation, the order in which the social variables were entered into the model was changed to the following: 1) Non-Social Non-Linguistic, 2) Social-Linguistic, 3) Social Non-Linguistic, and 4) Social-Emotional. As expected, when Social-Linguistic was entered into the model as the first social predictor, it significantly predicted group membership (χ^2 (1) = 6.030, p = .014). As before, when the Social Non-linguistic (χ^2 (1) = 1.869, p = .172) and Social-Emotional (χ^2 (1) = .256, p = .613) predictors were added to the model, all variables including Social-Linguistic (χ^2 (1) = .933, p = .334) "lost" their individual predictive ability, even though the overall model remained significant (χ^2 (4) = 9.760, p = .045).

Odds ratios in the final model help us interpret the strength of each predictor in contributing towards assignment of group membership. To aid in interpretation of odds ratios, pupillary variables were multiplied by 10 such that a one-unit change in the predictor variable equals 1/10th of a mm, a more appropriate metric for change in pupil dilation (it should be noted here that this conversion does not impact statistical significance or results in any way, but is merely a change in units). The largest effect was observed for the Social Non-Linguistic predictor in which a .1 mm increase in pupil diameter increase the odds of being in the TD group 1.85 times. Similarly, but to a smaller degree, every .1 mm increase in pupil diameter in the Social-Linguistic condition increased the likelihood of being in the TD group 1.54 times. The Social-Emotional condition (e^B = .803) and Non-Social Non-Linguistic (e^B = .800) conditions did not appear to increase the likelihood of TD membership.

To understand the respective influences of each of the social variables on classification accuracy, each variable was entered into a logistic regression as a separate model (see Table 6). Each social variable resulted in a model that significantly predicted group membership; however, Social Non-Linguistic and Social-Linguistic had larger odds ratios (1.82 and 1.84, respectively), and smaller *p*-values (.009, .012, respectively) than the Social-Emotional Condition (OR = 1.50, p = .051). Furthermore, Nagelkerke R^2 values indicate that Social Non-Linguistic (R^2 = .140) and Social-Linguistic (R^2 = .127) accounted for almost twice as much variance as the Social-Emotional condition (R^2 = .075).

Table 6.
Logistic Regression Analysis of Social Variables as Predictors of Group Membership.

Model	**Predictor**	**B**	**SE B**	**Wald's χ^2**	***df***	***p***	**e^B (Odds Ratio)**
1	Social Non-Linguistic	.600	.228	6.910	1	.009	1.822
				χ^2	***df***	***p***	**Nagelkerke R^2**
Model 1 Evaluation:				7.846	1	.005	.140
2	Social-Linguistic	.607	.243	6.245	1	.012	1.835
				χ^2	***df***	***p***	**Nagelkerke R^2**
Model 2 Evaluation:				7.061	1	.008	.127
3	Social- Emotional	.408	.209	3.800	1	.051	1.504
				χ^2	***df***	***p***	**Nagelkerke R^2**
Model 3 Evaluation:				4.107	4	.043	.075

* Hosmer & Lemeshow's goodness-of-fit tests were insignificant (p > .05) at each step of the model.

Table 7.
Observed and Predicted Frequencies for Group Membership

	Predicted		
Observed	**ASD**	**TD**	**% Correct**
Step 1: NSNL			
ASD	32	7	82.1
TD	26	6	18.8
Overall			53.5
Step 2: NSNL, *SNL*			
ASD	30	9	76.9
TD	14	18	56.3
Overall			67.6
Step 3: NSNL, SNL, *SL*			
ASD	30	9	76.9
TD	16	16	50.0
Overall			64.8
Step 4: NSNL, SNL, SL, *SE*			
ASD	32	7	82.1
TD	15	17	53.1
Overall			69.0

* NSNL = Non-Social Non-Linguistic, SNL = Social Non-Linguistic, SL = Social-Linguistic, SE = Social-Emotional

Table 7 (above) displays the observed and predicted classification of individuals into either the ASD or TD group, for each iteration of the hierarchical regression. In the first step, with only Non-Social Non-Linguistic included as a predictor, the accuracy of prediction of group membership was not significantly above chance, or more accurate than the null model. In the null model, all participants were categorized into the ASD group resulting in 100% accuracy for the ASD group, and 0% accuracy for the TD group (overall = 54.9%). In Step 1, the addition of the Non-Social Non-Linguistic variable does not improve the overall accuracy; however, group membership is redistributed so that TD group prediction improves to 18%. When the Social Non-Linguistic condition was added in Step 2, there was a 14% increase in the overall predictive power of the model and the predictiveness for the TD group improved to slightly above chance (56%). In the final model, with all variables included, individuals with ASD were correctly classified with greater than 80% accuracy; roughly a 30% improvement over grouping that would occur by chance. However, the predictive power of the model was relatively poor for the TD group, with only 53% of TD individuals correctly classified, a figure that is comparable to chance.

Objective 4 Results

The fourth and final study objective was to understand how pupillary responses might be related to real-world measures of ASD symptoms. Specifically, this included parent-report measures of ASD traits, sensory symptoms, social behaviours, and restricted interests and repetitive behaviours. Statistical reporting of results below are limited to significant and/or meaningful findings, a full report of all correlation coefficients and significance values can be found in Appendix C.

Hypothesis 7: Pupillary responses to social stimuli and ASD symptoms.

It was hypothesized that pupillary responses to social stimuli would have a negative association with ASD symptoms as they relate specifically to ASD traits, (as measured by the Autism Spectrum Quotient), problems in social behaviour (as measured by the Social Responsiveness Scale - 2nd Edition), and restricted and repetitive interest and behaviours (as measured by the Repetitive Behaviours Questionnaire - 2nd Edition). The direction of this relationship was expected to be similar for both typically developing children and children with ASD, although the observed correlations may be limited by a lack of variance in the TD group. Results will be reported separately for each scale. For this hypothesis, only the relationship between synchronous stimuli and measures were observed, as hypothesis 8 and 9 pertain more directly to the relationships with asynchronous conditions.

Autism spectrum quotient – children's version (AQ).

Descriptive statistics for the AQ-Child are reported in Table 8, which includes values for the total scale and each of the 5 subscales that relate to different traits characteristic of ASD. Authors of the AQ-Child recommend a cut-off value of 76 when using the measure as a screener for ASD (Auyeung et al., 2008). As expected, a majority of the ASD group scored above this cut-off (~79%), whereas only ~6% of the TD group scored above this cut-off. There were no significant relationships ($p > .05$) between synchronous social stimuli (Social-Linguistic, Social Non-Linguistic, or Social-Emotional) and the AQ total score, or between any of the subscales for either group.

Table 8.
Descriptive Statistics for Autism Spectrum Quotient – Children's Version

Total N = 70	**ASD (Total N = 38)**	**TD (Total N = 32)**
	M (SD)	
AQ Total Score Max score = 150	94.1 (17.9)	51.7 (13.1)
Scored Above Cut-off (76)	78.9% (n = 30)	6.3% (n = 2)
AQ Subscales		
Social Skills	19.7 (5.4)	8.3 (4.6)
Attention Switching	20.6 (4.9)	10.8 (3.7)
Attention to Detail	15.0 (6.9)	14.6 (4.3)
Communication	22.1 (5.5)	8.2 (4.1)
Imagination	16.7 (5.5)	9.8 (3.6)

Social Responsiveness Scale – 2nd Edition (SRS).

Descriptive statistics on the SRS-2 are included in Table 9. As with the AQ, authors of the SRS, suggest a cut-off value for clinically significant ASD symptoms. In the ASD group, ~92% of the sample scored above this cut-off, and ~22% of the TD sample also scored above this cut-off. In the ASD group there was a significant negative correlation between the Social-Emotional condition and the Social Awareness subscale of the SRS ($r = -.340$, $p = .037$). That is, smaller pupillary responses were associated with a higher level of autistic tendency on this scale. The Restricted Interests and Repetitive Behaviours (RRB) subscale was significantly negatively correlated with all three social conditions: Social-Linguistic ($r = -.366$, $p = .024$), Social Non-Linguistic ($r = -.356$, $p = .028$), and Social-Emotional ($r = -.461$, $p = .004$). All other relationships between subscales and conditions yielded were insignificant in the ASD group. In the TD group, there was only one significant relationship, which occurred between the Social-Emotional condition and the Social Awareness subscale ($r = .377$, $p = .033$); it was unexpected and contrary to predicted hypotheses that this relationship was positive in nature for the TD group. Figure 10 (below) depicts the relationships between these two variables for ASD and TD groups.

Table 9.

Descriptive Statistics for Social Responsiveness Scale – 2

Total N = 70	**ASD (Total N = 38)**	**TD (Total N = 32)**
	Raw Scores M (SD)	
SRS Total Score	109.1 (31.9)	40.0 (25.7)
Scored above cut-off for clinically significant symptoms (57 for males, 51 for females)	92.1% (n = 35)	21.9% (n = 7)
SRS Treatment Subscales		
Social Awareness	13.6 (4.2)	6.5 (2.7)
Social Cognition	20.4 (6.8)	7.5 (5.8)
Social Communication	37.2 (11.4)	11.7 (9.2)
Social Motivation	16.7 (6.4)	7.9 (5.2)
DSM-5 Compatible Scales		
Social Communication & Interaction (SCI)	87.8 (26.1)	33.6 (20.1)
Restricted Interests and Repetitive Behaviours (RRB)	21.2 (7.1)	6.3 (6.3)

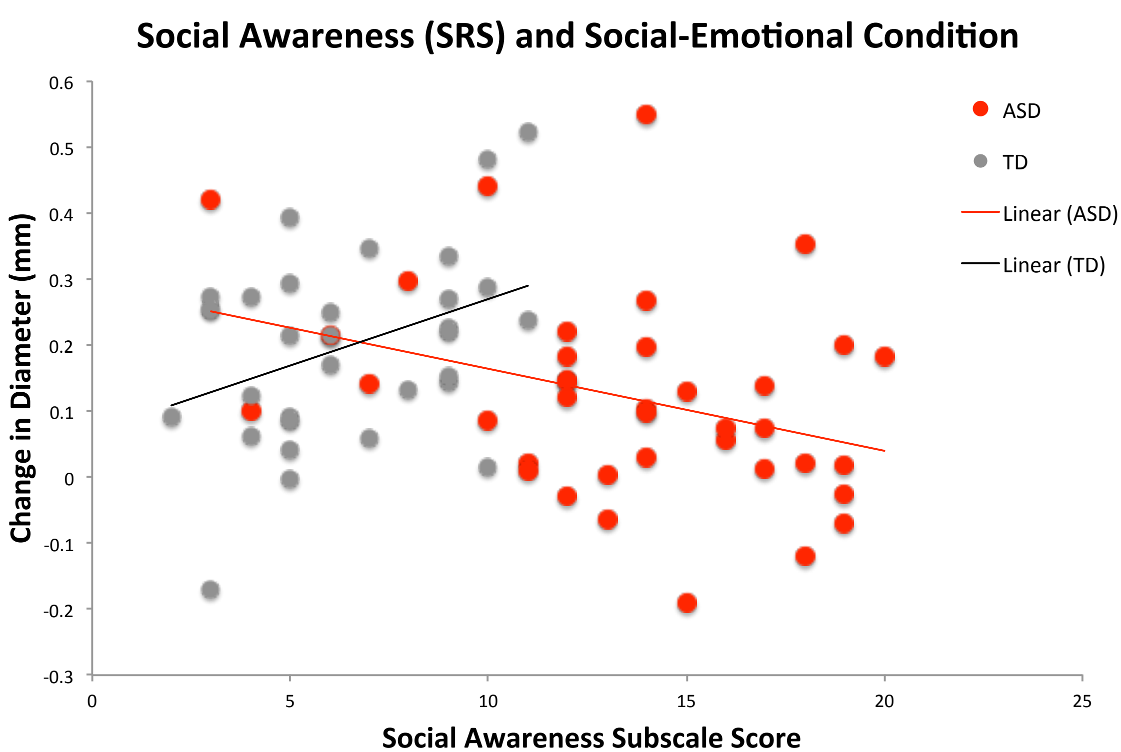

Figure 10. Scatterplot portraying relationship between scores on the SRS social awareness subscale and pupillary response for the social-emotional condition.

Repetitive Behaviour Questionnaire – 2nd Edition (RBQ-2).

Descriptive statistics for the RBQ – 2 are displayed in Table 10. The RBQ does not have assigned cut-off scores; however, authors have suggested 2-factor and 4-factor models for interpreting subscale scores. For the ASD group, correlations between Social conditions and the RBQ total score ranged from -.29 to -.31 but did not reach statistical significance at the $p < .05$ level. In the TD group, Pearson r values for the RBQ total score were close to zero and did not approach statistical significance.

Table 10.

Descriptive Statistics for Repetitive Behaviour Questionnaire – 2

Total N = 70	**ASD (Total N = 38)**	**TD (Total N = 32)**
	Raw Scores M (SD)	
RBQ Total Score	32.7 (9.4)	23.9 (5.6)
RBQ 2 – Factor		
1 - Motor/Sensory Behaviours	14.1 (5.1)	11.4 (3.5)
2 - Rigidity/Routines/ Preoccupation with Restricted Interests	14.8 (4.6)	10.1 (2.9)
RBQ 4 – Factor		
1 – Repetitive Motor Movements	8.1 (3.1)	6.4 (2.4)
2 – Rigidity/Adherence to Routine	13.0 (3.9)	8.6 (2.7)
3 – Preoccupation with Restricted Patterns of Interest	12.2 (4.2)	9.1 (2.8)
4 – Unusual Sensory Interest	6.3 (2.4)	5.0 (1.4)

Hypothesis 8: Pupillary responses to asynchronous stimuli and ASD symptoms

Hypothesis 8 relates to the relationships between ASD symptoms and pupillary responses to asynchrony. Based on previous studies in our lab, in which individuals with ASD differed in their responses to asynchrony from TD children (Bebko et al., 2006), it was expected that greater response to asynchrony would be negatively associated with measures of ASD symptoms. Relationships between ASD symptoms and pupillary response to asynchrony were not expected to be significant for the TD group. To minimize the number of correlations being performed, AV (audio-leading) and VA (visual-leading) conditions were combined and treated as one "asynchrony" category.

Autism spectrum quotient – children's version (AQ).

For the ASD group, there were significant negative correlations that emerged on the Communication subscale of the AQ between the Social-Linguistic (r = -.349, p = .032), Social Non-Linguistic (r = -.425, p = .008), and Social-Emotional subscales (r = -.415, p = .009). Correlations between AQ scores and the Non-Social Non-Linguistic condition did not reach or approach significance on any subscales. Conversely, in the TD group, a significant *positive* correlation was observed between the Non-Social Non-Linguistic condition and the AQ total score (r = .423, p = .016) and the Attention Switching (r = .455, p = .009) and Communication subscales (r = .400, p = .023).

Social Responsiveness Scale – 2nd Edition (SRS).

Results for relationships between asynchronous social conditions and the SRS were similar to the above reported relationships for synchronous presentations (Hypothesis 7). Negative relationships were observed between the Social-Emotional condition and the SRS total score (r = -.342, p = .036), the Social Awareness Subscale (r = -.336, p = .039), the Social Cognition subscale (r = -.346, p = .033), and the Restricted and Repetitive Behaviours subscale (r = -.502, p = .001). The Restricted and Repetitive Behaviours subscale was also correlated significantly with the Social-Linguistic condition (r = -.320, p = .050) and the Social Non-Linguistic condition (r = -.470, p = .003), but not with the Non-Social Non-Linguistic condition (r = -.261, p = .113). No other relationships were statistically significant.

In the TD group, relationships between SRS scores and social asynchronous conditions were all in a positive direction; however, none of these relationships were significant at the p <

.05 level. Interestingly, for the Non-Social Non-Linguistic asynchronous condition, there was a significant positive relationship with the SRS total score (*r* = .486, *p* = .005). Correlations between the Non-Social Non-Linguistic asynchronous condition were significant for each subscale on the SRS with Pearson *r* values ranging from .384 - .554 (*p* = .001 - .030).

Repetitive Behaviour Questionnaire – 2nd Edition (RBQ-2).

No significant correlations between pupillary response to asynchronous conditions and scores on the RBQ were observed for either group.

Hypothesis 9: Pupillary responses and sensory processing

The final hypothesis is focused on the relationships between pupillary responses to experimental stimuli and sensory processing as measured by the Child Sensory Profile-2. Table 11 displays descriptive statistics for the total score and three categories of subscales as proposed by the authors: quadrant subscales, sensory subscales, and behavioural subscales.

Table 11.
Descriptive Statistics for Child Sensory Profile – 2.

Total N = 70	**ASD (Total N = 38)**	**TD (Total N = 32)**
	Raw Scores M (SD)	
SP Total Score	210.0 (71.4)	122.0 (55.4)
SP Quadrant Subscales		
Seeking/Seeker	40.6 (21.9)	27.9 (14.0)
Avoiding/Avoider	55.9 (16.3)	28.8 (14.7)
Sensitivity/Sensor	51.9 (17.6)	27.2 (12.8)
Registration/Bystander	50.6 (18.5)	27.5 (14.4)
SP Sensory Subscales		
Auditory	23.7 (7.6)	12.2 (7.7)
Visual	14.1 (5.4)	11.0 (5.0)
Touch	22.4 (12.2)	12.4 (8.2)
Movement	15.4 (9.5)	9.8 (6.1)
Body Position	16.3 (9.1)	10.3 (5.3)
Oral	25.2 (14.8)	18.4 (11.4)
SP Behavioural Subscales		
Conduct	22.1 (10.3)	12.7 (7.6)
Social Emotional	42.3 (11.2)	20.9 (12.5)
Attentional	25.4 (10.6)	12.3 (7.9)

Several significant correlations emerged on the Sensory Profile for the ASD group (see Appendix C, Table C7). The pattern and strength of results were comparable between correlations for synchronous and asynchronous presentations. Since there was no evidence of a unique relationship to asynchrony on the SP, conditions were collapsed across synchrony and are presented here as combined categories. Interestingly, the majority of significant relationships were within the social conditions, with most of the correlations for the Non-Social Non-Linguistic category being relatively weak. Correlations were strongest in the Social Non-Linguistic and the Social-Emotional conditions, particularly within the quadrant and behavioural subscales. In general, this pattern of negative correlations indicates that smaller pupillary responses to social information were associated with higher scores on the SP indicative of a higher degree of sensory impairment. As expected, no evidence of an association between pupillary responses and sensory processing emerged within the TD group with correlations ranging from $r = .007 - .29$ ($p > .10$; see Appendix B).

Discussion

The main goal of this study was to understand the process by which multisensory social information is processed in children with Autism Spectrum Disorder (ASD), a clinical population characterized by impairments in social interactions. This study included several novel additions to the pupillometry literature including being the first study to use audiovisual presentations of social and non-social stimuli that were realistic and representative of real-world experiences. As expected, the results of this study indeed suggest that individuals with ASD differ from chronological and mental age-matched TD children in their physiological and cognitive responses to social information, but not to non-social information. Further, smaller pupillary responses to social information in ASD were associated with increased ASD symptomatology including parent report ratings of social competence and sensory processing. Pupillary responses were able to reliably predict group membership for children with ASD with a high degree of accuracy, indicating that pupillary responses to social information have value as a potential biomarker for identification of ASD. Overall, the results of this study confirm that pupillary response to social information not only reflects atypical cognitive processing of social information in ASD, but that the response is also associated with impairments in social and sensory processing.

The current study was the first of its kind to explore the role of audiovisual temporal processing using pupillary responses as a correlate of cognitive activity. While the overall magnitude of pupillary response between TD and ASD participants differed, the pattern of response to synchronous and asynchronous stimuli was the same. These results indicate that there may be aspects of temporal processing which are intact, or unaffected in ASD. The implications of these results are explored further below.

Pupillary Response to Social and Non-Social Stimuli

The most significant finding in response to stimuli was the difference between TD and ASD in pupillary responses to social information. For all social conditions (linguistic, non-linguistic, emotional) typically developing children had significantly greater pupil dilations than children with ASD. Few pupillary studies have directly compared the response to social information and non-social information in ASD. Here, in conditions that closely approximate the complexity and stimulating aspects of a real-world setting, social information remains less engaging for individuals with ASD. The results of this study are consistent with Anderson et al., (2006) who observed decreased dilation to human faces in ASD when compared to TD individuals, but in response to visual-only, still photographs. This finding is particularly meaningful when considered in the context of observed pupillary responses to non-social information. In contrast to social stimuli, there were no differences between groups when measuring responses to non-social information. A similar pupillary response to moving objects (non-social condition) between groups rules out the interpretation that pupillary responses were simply larger across the board in typical development. Interestingly, in typical development there was no differentiation in pupillary response across stimuli, as dilation was similar between social and non-social conditions. However, in ASD, there was a larger response to non-social information, compared to social information, which is in line with theoretical and *a priori* expectations. Therefore, while all stimulus types resulted in comparable levels of arousal or cognitive engagement in TD, children with ASD showed attenuated responses to social information, which is associated with lower levels of engagement.

The apparent lack of interest or engagement in social stimuli is a robust and consistent finding in ASD research, one which has been demonstrated in retrospective studies of early childhood (Baranek, 1999; Osterling & Dawson, 1994) and gaze patterns in eye-tracking studies (Bebko et al., 2006; Jones et al., 2016; Klin, Jones, Schultz, Volkmar, & Cohen, 2011). Performance and responses in behavioural paradigms also indicate slower reaction times (Corden, Chilvers, & Skuse, 2008), impaired memory (Williams, Goldstein, & Minshew, 2005) and decreased performance on tasks using social stimuli (Mongillo et al., 2008; Stevenson et al., 2014c) in ASD. Corroboration of an atypical response to social stimuli in pupillary response provides evidence that pupillometry is a sensitive and reliable indicator of underlying cognitive processes associated with core impairments in ASD.

Another goal of this study was to explore differences within social stimuli to determine whether particular aspects of social stimuli (language or emotion) had unique effects on pupillary response. While overall response to social conditions was greater in TD, the *pattern* of responding was the same for both groups. That is, there were comparable pupillary responses to conditions containing purely social information and those including language, and an increased response to conditions including emotional (happy and sad) information for both groups. This indicates that for both TD and ASD children, stimuli containing emotional cues were more arousing than the other social conditions. These results partially support the *a priori* hypothesis that predicted the largest change in dilation to emotional conditions; however, it was also expected that the next most socially relevant condition (social-linguistic) would elicit the next largest response. Interestingly, pupillary response to the social-linguistic condition, which might be considered more information-rich and complex, as it contains speech signals and content, did not differ from the social non-linguistic condition (nonsensical sounds) for either group. This is in contrast to studies that have demonstrated greater pupillary response to syntactically complex sentences compared to simple sentences (Just & Carpenter, 1993). However, it may be that in this case, the novelty of the social non-linguistic stimuli (person making various sounds such as kissing, hissing, lip-smacking, etc.) may have accounted for a comparable response to the language rich information or that the social non-linguistic stimuli provided a different category of perceptual complexity.

Although this study did not test for recognition of specific emotions, there was a clear response in both groups suggesting that the emotional content (happy and sad) was more arousing than other social conditions. There is some controversy regarding the ability to recognize emotions in ASD with evidence for (Feldman, McGee, Mann, & Strain, 1993; Harms, Martin, & Wallace, 2010; Hobson, Ouston, & Lee, 1988; Ozonoff, Pennington, & Rogers, 1990) and against (Castelli, 2005; Loveland et al., 1997; Robel et al., 2004; Rosset et al., 2008) impaired emotion recognition. Regardless of the accuracy of emotional identification (which may translate more readily into real-world social impairments), there was nevertheless a physiological response to emotion that exceeded response to non-emotional social stimuli in ASD. A greater response to emotionally-valenced stimuli has been documented in typical development (Bradley et al., 2008; Libby et al., 1973; Partala et al., 2000; Stanners et al., 1979); however, studies including ASD participants have had mixed results. Wagner and colleagues (2013) found no difference in pupillary response to fearful or happy faces when compared to neutral faces for both TD and ASD participants. Similarly, another study comparing pupillary dilation in ASD and TD to happy, angry, fear, and neutral expressions did not find between-group differences in pupillary response to emotions or significant differences between neutral and negatively or positively-valenced emotions (Sepeta et al., 2012). In contrast, and more in line with the results of the current study, Nuske et al., (2014) found that typically developing participants had a significantly greater pupillary dilation to fearful expressions of unfamiliar people than participants with ASD. Given the social and evolutionary significance of recognizing and responding to emotionally-charged faces, it was expected and reasonable that emotional faces elicited a physiological reaction in both typical and atypical development. The greater pupillary response observed in typical development as opposed to in ASD, likely has a relationship to the ability to be aware of, recognize, and respond appropriately to these cues in everyday environments that is most certainly more developed in typically developing participants.

Relationship of Pupillary Response to ASD Symptomatology and Diagnosis

Associations between pupil dilation and measures of social impairment and restricted and repetitive behaviours in ASD.

Correlational analyses generally supported *a priori* hypotheses for negative associations between pupillary response (especially to social stimuli) and severity of ASD symptoms. Autistic traits specifically related to communication, as measured by the AQ-Child, had a moderate negative relationship with *asynchronous social conditions*. That is, smaller pupillary responses to asynchronous social conditions were related to greater communication impairments, which may translate into skills such as understanding etiquette, engaging in and following conversational rules, reading interpersonal cues, and understanding jokes. It is somewhat surprising that the above relationship was stronger for asynchronous than synchronous presentations. One possibility is that there may be a stronger relationship between the ability to recognize and respond to temporal synchrony in social stimuli and real-world social behaviours. Perhaps greater *sensitivity* to social information, in general, is related to greater social awareness and correspondingly, a decrease in social impairment. For instance, just as individuals who are more sensitive to subtle social cues and behaviours (e.g., glances, expressions, conversational pauses) likely have greater social competence, perhaps sensitivity to discrepancies in audiovisual cues (e.g., mismatched timing of speech sounds and mouth movements) is similarly related to higher social skills. Thus, a reasonable interpretation of the relationships observed in these data are that improved temporal processing of social information is linked to better social skills in children with ASD.

To the author's knowledge, this study is the first to report on a relationship between temporal multisensory processing and ASD symptoms within individuals with ASD. However, a study examining autistic traits within typical developing populations established an association between abnormal temporal processing for low-level audiovisual stimuli (tones and black and white checkerboard pattern) and the total score on the AQ (Donohue, Darling, & Mitroff, 2012). This finding seems to lend support for the hypothesized theory that disrupted temporal processing will have negative implications on real-world experiences, particularly within the social domain.

There appeared to be no significant associations between measures of pupillary response to any condition (synchronous or asynchronous) and restricted and repetitive behaviours as measured by the RBQ-2. Items on the RBQ-2 generally fall into one of two factors, which measure motor and sensory behaviours (e.g., arranging toys, spinning, rocking, visual inspection of objects) and rigidity, routines, and preoccupations with restricted interests. Interestingly, there were moderate negative associations between pupillary response on the Restricted and Repetitive Behaviour subscale of the Social Responsiveness Scale. While there is a high degree of similarity between items on the RBQ-2 and the RRB subscale of the SRS, it is possible that some items on the SRS have a slightly more social quality (e.g., is regarded by other children as odd or weird, touches others in an unusual way), which accounted for a slightly stronger relationship to pupillary responses.

The social-emotional condition was also related to more socially-oriented subscales on the SRS, particularly for asynchronous presentations. The SRS Total Score, Social Awareness subscale, and Social Cognition subscale had significant negative correlations with pupillary response to emotional stimuli, whereas correlations between these scales and the other social conditions were not significant. Relationships between pupillary responses in the social-emotional condition and the behaviours measured by the above scales indicate that physiological response to emotion is perhaps more strongly related to actual social competence than pupillary responses to speech (Social-Linguistic) or arbitrary noises (Social Non-Linguistic), even within a social context (facial stimuli). It is logical that reactions (pupillary or otherwise) to social-emotional information are more strongly related to social competence, as many of the areas being assessed by the SRS include sensitivity of and awareness to emotional reactions in others (e.g., is aware of what others are thinking or feeling, is able to understand the meaning of other people's tone of voice and facial expressions). These results seem to agree with findings reported by Erstenyuk and colleagues (2014), who demonstrated that typically developing children with higher social impairment (as measured by the SRS) showed smaller pupil dilation to an ambiguous joint attention task, which involved following of eye-gaze. Erstenyuk and colleagues (2014) suggested that children with lower social abilities might be overwhelmed by the demands associated with an ambiguous social task, leading to disengagement and under-arousal. The directional nature of this proposed relationship; however, remains unclear, as it seems equally plausible that children with higher social impairment are less aware, and therefore less respondent to social stimuli, *or* that the higher level of difficulty associated with the task results in a reduced inclination to allocate cognitive resources to interpreting the information at hand (Erstenyuk et al., 2014). In a study with children with autism, Nuske and colleagues (2014) found a relationship between peak pupillary latency to fearful expressions of unfamiliar people and prosocial behaviour (as measured by the Empathy Questionnaire; Rieffe, Ketelaar, & Wiefferink, 2010), indicating that quicker pupillary responses to emotion was related to more empathic behaviour. Pupillary activity was also related to the communication and play algorithm on the ADOS, such that greater pupil dilation to the emotional expressions of familiar people was associated with fewer deficits in those symptom domains (Nuske et al., 2014b). Therefore, the evidence seems to suggest that greater pupillary response to social information, particularly emotional stimuli, is related to improved social competence and fewer ASD-related symptoms both in ASD and typical development.

Associations between pupil dilation and sensory processing in ASD.

Similarly to relationships on other parent-report measures in this study, significant relationships between pupillary responses and scores on the Child Sensory Profile (SP) tended to occur in the social conditions, with only one significant correlation emerging in the non-social non-linguistic condition. All the correlations observed were negative relationships ranging from weak to moderate in strength. Though there were several significant relationships in the social-linguistic condition, the majority of significant relationships emerged in the social non-linguistic and the social-emotional conditions, both of which were moderately correlated with the SP total score. The direction and high number of significant relationships observed speak to the credibility of a genuine association between pupillary response and sensory processing.

Subscales on the SP are grouped into three domains, which will be discussed in turn: Quadrant subscales, Sensory subscales, and Behavioural Subscales.

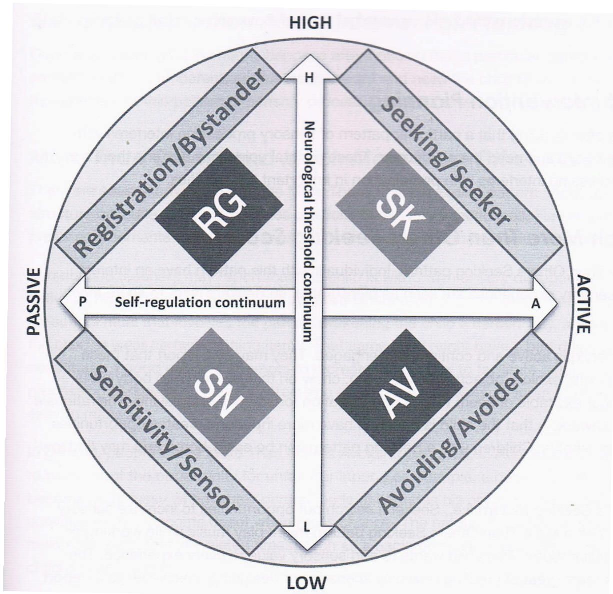

Figure 11. Dunn's Sensory Processing Framework.

Quadrant scores are comprised of four subscales that fall along two continuums, the neurological threshold (the nervous system's level of responsiveness to stimuli) and the self-regulation continuum (the level that the individual attempts to control the amount and type of sensory input; see Figure 11). Of the Quadrant scores, the *Seeking* subscale, which is characterized as high threshold and active self-regulation, had the strongest negative correlations with pupillary responses in all three social conditions. Individuals scoring high on this scale tend to seek out higher intensity sensory input in ways that might be excessive or disruptive. While the relationship on the Seeking subscale might be slightly stronger than others, no one pattern of sensory processing appeared to have a unique association with pupillary response. Rather, this implies that any extreme or atypical pattern of responding to sensory stimuli, whether hypo- or hyper-sensitive, overly active or passive, is associated with a greater departure from normative autonomic arousal (i.e., smaller pupil dilation compared to normative development).

The sensory subscales on the SP address separate sensory systems including: auditory, visual, touch, movement, body position, and oral sensory processing. Somewhat surprisingly auditory and visual domains were not associated with pupillary response, and the movement domain had moderate negative correlations with all social conditions. Those who score highly on the movement subscale might be overly fidgety, take physical risks when playing, fall down on purpose, or be physically clumsy. Relationships also emerged on the touch (e.g., displays need to touch surfaces or textures) and oral processing (e.g., gags easily, strongly rejects or craves certain tastes or smells or food textures) subscales. The pattern of relationships between these particular sensory subscales and pupillary response to social conditions was unexpected. Perhaps these correlations are best explained as falling under the scope of the total score, in that abnormal sensory processing across a higher number of domains has a stronger relationship with atypical pupil dilation.

A similar interpretative approach is taken to the relationships that emerged within the SP behavioural subscales, which include scales related to conduct, social-emotional, and attentional responses associated with sensory processing. These subscales appear to relate more generally to difficulties that may result from atypical sensory processing, such as having temper tantrums (conduct), being too sensitive or serious (social-emotional), or struggling to pay attention in certain environments (attentional). These results concur with findings reported in a recent study examining pupillary light reflex and sensory behaviours (as measured by the Sensory Profile) in children with ASD (Daluwatte, Miles, Sun, & Yao, 2015). Specifically, Daluwatte and colleagues (2015) found that smaller constriction amplitudes (i.e., a reduction in response to light stimulus) were associated with more atypical sensory behaviours.

Associations between pupil dilation and measures of ASD symptoms in TD.

As expected, in the typically developing sample, there were no associations between pupillary responses and scores on measures of repetitive behaviours (RBQ-2) or sensory processing (SP-2), the latter congruent with Daluwatte et al (2015) who also reported no relationship to pupillary response and sensory processing in TD. However, there were several significant relationships between ASD traits (as measured by the AQ and the SRS) and pupillary responses but in the opposite direction from patterns observed in ASD participants. Based on a previous study, in which ASD traits in typical populations were related to abnormal pupillary processing (Erstenyuk et al., 2014), it was predicted that associations in TD would mirror those observed in ASD, or be non-existent due to a lack of variance. Contrary to expectations, in the TD group only, relationships to ASD traits tended to be in a positive direction; that is, larger pupillary responses were associated with higher autistic traits. Interestingly, with one exception, these associations were significant between *non-social non-linguistic* conditions and scores on the AQ and the SRS. This relationship was stronger for asynchronous stimuli; however, correlations with synchronous stimuli were in the same direction (positive) and approaching significance; therefore, it is more likely that this effect was driven by response to stimulus type, rather than manipulations of temporal synchrony. One possibility is that increased pupillary response to the non-social condition translates into a greater sensitivity to and engagement with object related stimuli. Perhaps heightened sensitivity to objects (and not people) is correlated with a higher presence of sub-clinical autistic traits among typically developing youth. Before accepting this interpretation, it is prudent to consider the validity of these relationships. Firstly, the majority of participants in the TD group were well below the assigned cut-off for clinical impairment for both the AQ (~94% below cut-off) and the SRS (~78% below cut-off). This indicates that even in the higher range of scores, TD participants were still within the normal range of behaviour, and were not rated as exhibiting clinically abnormal behaviour or significant social impairment, which may limit the merit of this relationship. Secondly, the data was inspected for outliers and the strength of these relationships may have been partially driven by some extreme cases. Two extreme cases were identified within each scale and correlations were re-run with outliers removed. Without the presence of these extreme scores, the total score on the AQ was no longer significantly associated with the non-social non-linguistic condition, and only one subscale (Attention Switching) remained significant (r = .433, p =.019). Removing outliers provided similar results on the SRS, with the total score no longer being statistically significant, and only one subscale retaining significance (Social Awareness, r = .464, p =.011). Replication of a similar paradigm will be necessary to determine the validity of the relationship between greater pupillary response to object stimuli and increase in ASD symptoms within typical development.

Group membership classification.

A logistic regression was performed to determine whether pupillary responses to experimental stimuli could successful predict group membership. With the inclusion of all study variables in the model, prediction accuracy for all participants reached 69%, significantly above chance. Results of the logistic regression indicated that the greatest predictive ability was to responses in the Social-Linguistic and Social Non-Linguistic conditions. The Social-Emotional condition was the next strongest predictor, while the Non-Social Non-Linguistic condition was insignificant and did not contribute to the prediction of group membership above chance. An important consideration here is that pupillary responses to realistic audiovisual social stimuli (as what was presented in this study) appear to have good *sensitivity*; children with ASD were correctly classified over 30% above chance rates. *Specificity* on the other hand was relatively poor, as classification for TD individuals was not above chance (53%). In light of this, pupillary response to social information likely has the greatest value as a screening tool to flag the presence of atypical cognitive processing and physiological arousal. However, given the high "false positive" rate in TD (almost half of TD individuals were classified into the ASD group), pupillary response should not be used as a singular diagnostic test.

Pupillary Response to Temporal Processing

The role of temporal processing has been implicated in impaired multisensory integration in ASD by a growing body of work (see Stevenson et al., 2015 for a review). Asynchronous presentations were included as a key variable in the current study with the goal of determining whether pupillary responses supported patterns observed through eye-tracking (Bebko et al., 2006; Lavoie, Hancock, & Bebko, in prep) and behavioural studies (Kwakye, Foss-Feig, Cascio, Stone, & Wallace, 2011; Stevenson et al., 2014c; Stevenson et al., 2012; Woynaroski et al., 2013). However, this study did not find between group differences in response to synchrony as was expected. Accordingly, further analyses to explore response to asynchrony were conducted on all participants. Two main findings emerged from the temporal processing analysis: 1) both groups showed greater pupillary response to audio-leading (AV) asynchronous conditions, and 2) results in the social-emotional condition were the exception to this rule with a significantly greater response to synchronous presentations, compared to both audio-leading and visual-leading (VA) conditions. The significance of these findings will be discussed in turn.

As stated, greater pupillary responses were observed in the audio-leading condition for social-linguistic, social non-linguistic, and non-social non-linguistic stimuli. Interestingly, pupillary responses to visual-leading presentations were either comparable to those observed for synchronous presentations or slightly smaller (observed in the non-social non-linguistic condition). This pattern of responding indicates that both TD and ASD individuals responded differentially to AV presentations, whereas VA presentations were not deemed as engaging, or perhaps not identified as being out of sync. While both asynchronous presentations were offset by 1 second, audio-leading stimuli are a more unnatural occurrence in the environment and tend to be perceived as a greater violation than visual-leading stimuli (Dixon & Spitz, 1980; Hillock et al., 2011). For example, we often observed a person's mouth moving before hearing speech sounds and see lightning strike before hearing thunder. The basic physical properties of sound and light (light travels faster than sound), have likely contributed to the development of a greater tolerance for situations in which visual stimuli occur before auditory stimuli in humans.

In the context of the current study's results, the first to examine pupillary response to asynchrony, a greater pupillary response to audio-leading stimuli fits with what is known about temporal dynamics and human sensitivity to the temporal relationships between sight and sound. It follows that auditory leading asynchrony was associated with an increase in cognitive processing load and/or engagement due to the conflicting nature of asynchronous sensory cues. Keeping in mind that pupillary responses were on the whole much smaller in ASD, and differences between synchronous and AV conditions were smaller, the described pattern of responding to auditory-leading stimuli occurred in *both* groups (see Appendix B). The implications of these results, while seemingly contradictory with related studies (Bebko et al., 2006; Lavoie, Hancock, & Bebko, in prep), may speak to some aspect of intact temporal processing in ASD at the physiological level despite being impaired at the perceptual/behavioural level. It should be noted that previous work (Bebko et al., 2006) demonstrated group differences (between TD and ASD) in temporal processing for social, but not non-social stimuli, which partially supports the finding of preserved processing in this study. However, replication is needed to determine the validity of these suggestions.

The second key finding from the temporal processing analyses was that in the social-emotional condition, a completely different response pattern was observed. For social conditions with the presence of emotion (in this case happy and sad), the greatest pupillary response occurred to synchronous presentations for both TD and ASD participants. Pupil dilation is particularly responsive to emotional arousal, a robust finding that has been well demonstrated in pupillometry research (Bradley et al., 2008; Partala et al., 2000; Stanners et al., 1979). Little is known about the multi-sensory integration of emotional cues, and it is possible that a different process is involved when emotion is present. Given the social and evolutionary significance of recognizing and responding to emotional cues in others, the synchronous emotional presentation may have “stood out” as particularly arousing because it was more meaningful than the asynchronous presentations. The emotional nature of this condition resulted in increased pupillary response in both groups for a number of possible reasons: 1) the social/evolutionary significance of emotional content, 2) the potentially confusing/distressing nature of asynchronous emotional stimuli requiring greater cognitive effort to process, and 3) the salience of synchronous emotional stimuli, more likely to elicit increased arousal in the participant. Considering social-emotional impairments characteristic in ASD, it is encouraging to observe similar patterns of responding to socially-relevant stimuli, suggesting some level of intact processing. Despite smaller pupillary responses to social stimuli overall, there appears to be some unconscious physiological responding in ASD linked to differing levels of significance (i.e., synchronous vs. asynchronous) within emotional stimuli.

Baseline Pupil Diameter and ASD

The purpose of the current study was to examine pupillary responses as an index of cognitive activity related to dynamic, multisensory stimuli in ASD. The validity of such experimental measurements is predicated on accounting for possible differences in resting or tonic pupil size between ASD and typically developing individuals. The results of this study coincide with a growing list of research studies reporting no difference in baseline pupil size (Fan et al., 2009; Nuske et al., 2014a; Nyström, Gredebäck, Bölte, & Falck-Ytter, 2015; Van Engeland et al., 1991), as opposed to studies reporting smaller (Martineau et al., 2011; Rubin, 1961) or larger (Anderson & Colombo, 2009; Anderson et al., 2013) pupil size in ASD. A lack of difference in tonic pupil size ensures that the observed results reported in this study are responses to experimental conditions and manipulations, and not simply due to a baseline difference in pupil size. Another important aspect in ensuring that pupillary responses were a result of experimental stimuli was the use of inter-stimulus fixation trials as a baseline for each condition. This procedure helped control for even slight variations in pupil size throughout the duration of the experiment and provide a more sensitive and temporally accurate measurement of pupillary change compared to the pre-experiment baseline.

Implications

Through careful control of study elements including standardization of luminance, timing of stimulus presentation, baseline-corrected analyses, inclusion of a range of stimulus types, and manipulation of temporal synchrony, the current study established pupillary response as a meaningful indicator of engagement and the cognitive processes involved in processing dynamic and complex stimuli. Furthermore, the current study offers several novel elements to the study of pupillometry in ASD. First, to the best of the author's knowledge, this is the first study to use dynamic, audiovisual stimuli instead of static or unisensory stimuli. The use of realistic videos greatly increases the ecological validity of these findings and allows for results to be more readily understood within real-world contexts. Second, this study was the first to examine pupillary response to temporal processing of multisensory information. Further, this study was able to make important discoveries regarding information processing in ASD, a clinical group known for a high degree of heterogeneity (Bruining et al., 2010; Lenroot & Yeung, 2013), through comparison to a chronological and mental age matched control group.

Overall, this study identified pupillary responses in ASD that differed from responses in children with typical development and corresponded with parent-reported measures of impairment. As predicted, individuals with ASD had a different response pattern to social stimuli (i.e., smaller magnitude of response), but were no different from controls for non-social stimuli. In understanding the current data, the observed pattern is most consistent with the engagement/arousal hypothesis of pupil dilation (Bradley et al., 2008). That is, typically developing individuals exhibited much greater pupillary responses to social information than individuals with ASD, which may be reflective of a greater level of interest in and awareness of social information. This interpretation also fits diagnostic criteria for ASD, specifically deficits in social-emotional reciprocity that often include failure to initiate or respond to social interactions and poor eye contact (APA, 2013). Others have described this apparent “lack of interest” in social stimuli as the *social motivation theory of autism*. The social motivation theory posits that typically developing humans are biased to *orient* towards social stimuli, be *rewarded* by engagement in social interactions, and strive to *maintain* social bonds (Chevallier et al., 2012). From an early age, many individuals with ASD display a robust lack of orienting to socially relevant stimuli (Klin et al., 2011; Nakano et al., 2010; Osterling & Dawson, 1994; Riby

& Hancock, 2008), paired with a preference for non-social stimuli (Pierce, Conant, Hazin, Stoner, & Desmond, 2011). According to the theory, by not orienting to and engaging in social stimuli, individuals with ASD are impoverished of social learning opportunities, which leads to impaired development of social skills and social cognition.

Interestingly, despite significantly reduced responding to social stimuli in ASD, it is important to note three *patterns* of responding in relation to specific stimuli that were similar to typically developing participants: 1) a greater overall response to emotionally-valenced stimuli compared to other social conditions, 2) greater response to audio-leading stimuli for social conditions containing either nonsense sounds or language, and the non-social condition, and 3) a greater response to synchrony for emotional conditions. The observed patterns suggest some degree of preserved or intact physiological response to social-emotional information and temporal relationships between visual and auditory cues. Interestingly, it has been demonstrated that, with explicit instruction to attend to social information individuals with ASD performed similar to controls on a variety of behavioural tasks (Senju, Southgate, White, & Frith, 2009; Wang, Lee, Sigman, & Dapretto, 2007; Whitehouse & Bishop, 2008). However, the same phenomenon has not necessarily been observed in studies exploring temporal processing. By nature, most temporal asynchrony detection tasks involve asking the participant to report whether the stimulus was in or out of synch (synchrony judgment task; SOJ) or the temporal order of the stimuli (temporal order judgment task; TOJ) and these consistently report impaired temporal processing in ASD (de Boer-Schellekens, Eussen, & Vroomen, 2013; Kwakye et al., 2011; Stevenson et al., 2014c). In eye-tracking studies, participants are typically not given instruction or cued to synchrony (Bebko et al., 2006; Lavoie, Hancock, & Bebko, in prep); however, a recent study reported that even when explicitly cued to search for the synchronous screen, participants with ASD did not perform comparably to controls (Grossman et al., 2015). Considerations of intact processes observed in this study, that may typically underlie perception and behaviour, will likely impact approaches to future interventions as well as provide a possible metric of progress. For instance, knowledge of specific areas of underdevelopment and preserved processing will help narrow the focus of interventions. Further, pupillary responding might be measured over time as an indicator of learning. For example, a social skills intervention might measure pupillary response to facial expressions prior to and following treatment as a measure of change.

The current study demonstrates the usefulness and feasibility of pupillary response as a possible biomarker of atypical processing. Early identification in ASD is critical and has significant implications for intervention planning and outcomes in later development. The non-invasiveness of pupillary measurement, requiring only passive viewing from the participant, lends itself well to use with very young children and has great potential as an early identification tool. Studies with infants and very young children will help determine whether atypical pupillary responses observed in ASD are a characteristic present in early life related to impaired social processing or if they are a product of the differential experiences of individuals with ASD and their social environment (i.e., reduced engagement in the social world). Given that the age range of the current study was from 6 to 20 years, it is unclear whether atypical pupillary processing of social information is a result or cause of social impairment and lesser social motivation. Studies with infants and young children will clarify the relationship of pupillary response in social processing and the order of this phenomenon. Nevertheless, this study predicted group membership for ASD individuals with 82% accuracy and adds to a growing list of studies that have demonstrated the capacity of pupillary responses to effectively predict presence of ASD

(Anderson & Colombo, 2009; Anderson et al., 2006; Martineau et al., 2011). While other researchers have explored the potential of pupillary light reflex to differentiate between atypical and typical development (Daluwatte et al., 2015; Daluwatte et al., 2013; Fan et al., 2009; Nyström et al., 2015; Rubin, 1961), the current study was able to do so via pupillary response to realistic social information. However, due to the fact that in the current study pupillary responses to stimuli resulted in poor specificity, caution should be exercised and further research is required before the full potential of pupillary measurement as a diagnostic tool is understood. Similarly, some caution should be used in the interpretation of correlational results, which identified a moderate negative relationship between pupillary responses to social information and ASD symptoms. While a substantive portion of the correlation analysis was determined a priori, a portion was exploratory, which resulted in the large number of correlations that were run. Given the increased risk of Type 1 error associated with increased number of analyses, these findings should be interpreted with care and replicated before these relationships are understood as genuine.

Directions for Future Research

The results of the current study represent important contributions to the fields of pupillometry and ASD research. It has been demonstrated that individuals with ASD show atypical pupillary response to social information when compared with typically developing children. Furthermore, these responses were correlated with ASD symptomatology that related specifically to deficits in social communication and sensory processing and significantly predicted diagnosis. However, there were several ambiguous findings that would benefit from replication, such as the positive relationship between ASD traits and pupillary response in typical development and the finding of intact temporal processing in ASD.

There were several limitations in the current study, which if addressed will strengthen future research. First, due to unexpected responses to the Piano condition, the number of presentations in the non-social non-linguistic condition was reduced by half. Therefore, despite intentions to vary the type of non-social stimuli presented, the non-social response was only based on pupillary responses to the Mousetrap condition. The finding of no difference in response to non-social stimuli between TD and ASD groups could be strengthened with the inclusion of a variety of non-social stimuli that adequately matches the complexity and number of audiovisual cues within social stimuli (e.g., speech). It should be noted here, however, that the effect sizes observed between groups with social stimuli were approximately ten times that observed with the non-social stimuli discussed here, suggesting that the reduced number of trials in the non-social Mousetrap condition does not likely account for the lack of significant group difference.

Another interesting consideration related to stimuli for future studies would be inclusion of people familiar to study participants, as familiarity is expected to impact the level of interest related to social stimuli. In fact, it has been demonstrated that inclusion of familiar faces improves matching of emotional expressions (Kahana-Kalman & Goldman, 2008), increases brain activation in the fusiform face area (Pierce & Redcay, 2008), and results in more normative pupillary response to expressions of fear (Nuske et al., 2014b) in ASD. Despite the need for significantly greater resources to make inclusion of individuals familiar to study participants possible, it would provide unique insight into social cognitive processes of individuals with ASD regarding people who are important and meaningful to them in their everyday lives.

Several other improvements should be considered in future work. First, future studies should include a synchrony judgment task so that unconscious physiological reactions can be compared with explicit reporting of perceptual judgments. Second, gaze data can be analyzed concurrently to understand better the relationship between physiological arousal and looking preferences. Third, an additional measure of arousal, such as galvanic skin response (GSR), could be collected simultaneously for comparison between different measures of psychophysiological response. Inclusion of all these critical pieces of information (i.e., pupillary response, gaze behaviours, and perceptual judgments) in one study will likely paint a more complete picture of the complex process that is temporal processing and perhaps illuminate some of the unanswered questions from this study.

Finally, a more uniform and balanced participant group would strengthen the conclusions and generalizations that could be made by this study. Specifically, this study encompassed a large age range (6 – 20yrs), was unbalanced in sex ratios between groups (77% male in the ASD group, 28% male in the TD group), and differed significantly on verbal IQ between groups. Resting pupil size has been shown to increase gradually over the first 20 years of life (MacLachlan & Howland, 2002) and decrease gradually from that point on (Birren, Casperson, & Botwinick, 1950; Winn, Whitaker, Elliott, & Phillips, 1994); this developmental change was controlled for with a repeated measures design, which compared each participant's pupillary change to his or her own baseline trials. However, a smaller age range would provide a more accurate indicator of pupillary change within a particular period of development. Furthermore, research with younger age groups will be necessary to move forward the potential of pupillary response as a possible bio-marker or screening tool for ASD. With regards to the uneven sex distribution, research suggests that pupillary responses do not vary by sex (Jones, 1990; Winn et al., 1994). Furthermore, it was shown in this study, that sex did not significantly predict pupillary response; therefore, it is unlikely that unbalanced sex groups impacted these results.

Nevertheless, future studies should aim to recruit greater balance between groups such that males and females are represented equally. With regards to IQ, future studies should consider a more comprehensive measure of intelligence than the abbreviated measure that was used in this study. A more robust measure will help elucidate the role of IQ, particularly the domain of verbal intelligence, and how it may have impacted the current results.

Conclusions

This study has provided a number of novel findings relating the physiological pupillary responses of individuals with ASD to audio-visual information. First, these data suggest that individuals with ASD demonstrate an attenuated pupillary response to social information, but not to non-social information. Importantly, the current study's use of dynamic stimuli with naturalistic audio-visual features contributes to the generalizability of the results. Second, in individuals with ASD, a reduction in pupillary response to social information was associated with greater impairments in social abilities and sensory processing as rated by caregivers. Third, pupillary responses to social information was used to reliably predict group membership for children with ASD, significantly above chance; indicating the usefulness of examining further pupillary response as a potential bio-marker for ASD identification. Fourth, this was the first study of its kind to examine pupillary responses to audiovisual temporal processing. These data suggest that patterns of responding in ASD mirrored typical physiological responses to synchronous and asynchronous stimuli. Measurement of pupillary responses is still a relatively new approach to understanding cognitive processing and physiological responses in individuals with ASD; the results of this study represent a significant contribution to our understanding of the value and interpretation of pupillary response and how it can be utilized in a unique clinical population such as ASD.

References

Adrien, J. L., Lenoir, P., Martineau, J., Perrot, A., Hameury, L., Larmande, C., & Sauvage, D. (1993). Blind ratings of early symptoms of autism based upon family home movies. *Journal of the American Academy of Child and Adolescent Psychiatry*, *32*(3), 617–626. http://doi.org/10.1097/00004583-199305000-00019

Anderson, C. J., & Colombo, J. (2009). Larger tonic pupil size in young children with autism spectrum disorder. *Developmental Psychobiology*, *51*(2), 207–211. http://doi.org/10.1002/dev.20352

Anderson, C. J., Colombo, J., & Shaddy, D. (2006). Visual scanning and pupillary responses in young children with Autism Spectrum Disorder. *Journal of Clinical and Experimental Neuropsychology*, *28*(7), 1238–1256. http://doi.org/10.1080/13803390500376790

Anderson, C. J., Colombo, J., & Unruh, K. E. (2013). Pupil and salivary indicators of autonomic dysfunction in autism spectrum disorder. *Developmental Psychobiology*, *55*(5), 465–482. http://doi.org/10.1002/dev.21051

Arnott, B., McConachie, H., Meins, E., Fernyhough, C., Couteur, A. Le, Turner, M., … Leekam, S. (2010). The frequency of restricted and repetitive behaviors in a community sample of 15-month-old infants. *Journal of Developmental and Behavioral Pediatrics : JDBP*, *31*(3), 223–229. http://doi.org/10.1097/DBP.0b013e3181d5a2ad

American Psychiatric Association. (2013). *Diagnositc and statistical manual of mental disorders (5th edition). Arlington, VA: American Psychiatric Publishing*.

Auyeung, B., Baron-Cohen, S., Wheelwright, S., & Allison, C. (2008). The Autism Spectrum Quotient : Children ' s Version (AQ-Child). *Journal of Autism and Developmental*

Disorders, *38*, 1230–1240. http://doi.org/10.1007/s10803-007-0504-z

Bachevalier, J., & Loveland, K. A. (2006). The orbitofrontal-amygdala circuit and self-regulation of social-emotional behavior in autism. *Neuroscience and Biobehavioral Reviews*. http://doi.org/10.1016/j.neubiorev.2005.07.002

Backs, R. W., & Walrath, L. C. (1992). Eye movement and pupillary response indices of mental workload during visual search of symbolic displays. *Applied Ergonomics*, *23*(4), 243–254. http://doi.org/10.1016/0003-6870(92)90152-L

Bahrick, L. E. (1992). Infants' perceptual differentiation of amodal and modality-specific audio-visual relations. *Journal of Experimental Child Psychology*, *53*(2), 180–199. http://doi.org/10.1016/0022-0965(92)90048-B

Bahrick, L. E., Netto, D., & Hernandez-Reif, M. (1998). Intermodal perception of adult and child faces and voices by infants. *Child Development*, *69*(5), 1263–1275. http://doi.org/10.2307/1132264

Baraldi, A. N., & Enders, C. K. (2010). An introduction to modern missing data analyses. *Journal of School Psychology*, *48*(1), 5–37. http://doi.org/10.1016/j.jsp.2009.10.001

Baranek, G. T. (1999). Autism during infancy: A retrospective video analysis of sensory-motor and social behaviors at 9-12 months of age. *Journal of Autism and Developmental Disorders*, *29*(3), 213–224. http://doi.org/10.1023/A:1023080005650

Beatty, J. (1982). Task-evoked pupillary responses, processing load, and the structure of processing resources. *Psychological Bulletin*, *91*(2), 276–292.

Beatty, J., & Lucero-Wagoner, B. (2000). *The pupillary system*. (J. T. Cacioppo, L. G. Tassinary, & G. G. Berntson, Eds.), *Handbook of psychophysiology*. Cambridge, MA: Cambridge

University Press. Retrieved from http://sunburst.usd.edu/~schieber/docs/Beatty_Pupillary_System_.pdf

Bebko, J. M., Schroeder, J. H., & Weiss, J. a. (2014). The mcgurk effect in children with autism and asperger syndrome. *Autism Research*, *7*(1), 50–59. http://doi.org/10.1002/aur.1343

Bebko, J. M., Weiss, J. a., Demark, J. L., & Gomez, P. (2006). Discrimination of temporal synchrony in intermodal events by children with autism and children with developmental disabilities without autism. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *47*(1), 88–98. http://doi.org/10.1111/j.1469-7610.2005.01443.x

Birren, J. E., Casperson, R. C., & Botwinick, J. (1950). Age changes in pupil size. *Journal of Gerontology*, *5*(3), 216–221. Retrieved from http://geronj.oxfordjournals.org/content/5/3/216.short

Bishop, D. V. (1998). Development of the Children's Communication Checklist (CCC): A method for assessing qualitative aspects of communicative impairment in children. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *39*(6), 879–891. http://doi.org/10.1017/S0021963098002832

Bradley, M. M., Miccoli, L., Escrig, M. a., & Lang, P. J. (2008). The pupil as a measure of emotional arousal and autonomic activation. *Psychophysiology*, *45*(4), 602–607. http://doi.org/10.1111/j.1469-8986.2008.00654.x

Brock, J., Brown, C. C., Boucher, J., & Rippon, G. (2002). The temporal binding deficit hypothesis of autism. *Development and Psychopathology*, *14*(2), 209–224. http://doi.org/10.1017/S0954579402002018

Brown, C., & Dunn, W. (2002). *Adolescent-adult sensory profile: User's manual*. San Antonio:

Therapy Skill Builders.

Bruining, H., de Sonneville, L., Swaab, H., de Jonge, M., Kas, M., van Engeland, H., & Vorstman, J. (2010). Dissecting the clinical heterogeneity of autism spectrum disorders through defined genotypes. *PLoS ONE*, *5*(5). http://doi.org/10.1371/journal.pone.0010887

Bruni, T. P. (2014). Test Review: Social Responsiveness Scale-Second Edition (SRS-2). *Journal of Psychoeducational Assessment*, *32*(4), 365–369. http://doi.org/10.1177/0734282913517525

Castelli, F. (2005). Understanding emotions from standardized facial expressions in autism and normal development. *Autism: The International Journal of Research and Practice*, *9*(4), 428–449. http://doi.org/10.1177/1362361305056082

Charbonneau, G., Bertone, A., Lepore, F., Nassim, M., Lassonde, M., Mottron, L., & Collignon, O. (2013). Multilevel alterations in the processing of audio-visual emotion expressions in autism spectrum disorders. *Neuropsychologia*, *51*(5), 1002–1010. http://doi.org/10.1016/j.neuropsychologia.2013.02.009

Chevallier, C., Kohls, G., Troiani, V., Brodkin, E. S., & Schultz, R. T. (2012). The social motivation theory of autism. *Trends in Cognitive Sciences*. http://doi.org/10.1016/j.tics.2012.02.007

Colombo, J. (1995). On the neural mechanisms underlying developmental and individual differences in visual fixation in infancy: Two hypotheses. *Developmental Review*, *15*, 97–135.

Constantino, J., & Gruber, C. (2002). *The social responsiveness scale*. Los Angeles, CA.: Western Psychological Services. Retrieved from http://www.giuntios.it/it/catalogo/SR011

Constantino, J. N., & Gruber, C. P. (2012). *Social Responsiveness Scale™, Second Edition (SRS™-2)*. Los Angeles, CA.: Western Psychological Services. Retrieved from http://www.wpspublish.com/store/p/2994/social-responsiveness-scale-second-edition-srs-2

Cooper, R. P., & Aslin, R. N. (1990). Preference for infant-directed speech in the first month after birth. *Child Development*, *61*(5), 1584–1595. http://doi.org/10.1111/j.1467-8624.1990.tb02885.x

Corden, B., Chilvers, R., & Skuse, D. (2008). Avoidance of emotionally arousing stimuli predicts social – perceptual impairment in Asperger ' s syndrome. *Neuropsychologia*, *46*, 137–147. http://doi.org/10.1016/j.neuropsychologia.2007.08.005

Daluwatte, C., Miles, J. H., Christ, S. E., Beversdorf, D. Q., Takahashi, T. N., & Yao, G. (2013). Atypical pupillary light reflex and heart rate variability in children with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *43*(8), 1910–1925. http://doi.org/10.1007/s10803-012-1741-3

Daluwatte, C., Miles, J. H., Sun, J., & Yao, G. (2015). Association between pupillary light reflex and sensory behaviors in children with autism spectrum disorders. *Research in Developmental Disabilities*, *37*, 209–215. http://doi.org/10.1016/j.ridd.2014.11.019

de Boer-Schellekens, L., Eussen, M., & Vroomen, J. (2013). Diminished sensitivity of audiovisual temporal order in autism spectrum disorder. *Frontiers in Integrative Neuroscience*, *7*(February), 8. http://doi.org/10.3389/fnint.2013.00008

Dixon, N. F., & Spitz, L. (1980). The detection of auditory visual desynchrony. *Perception*, *9*(6), 719–721. http://doi.org/10.1068/p090719

Donohue, S. E., Darling, E. F., & Mitroff, S. R. (2012). Links between multisensory processing and autism. *Experimental Brain Research*, *222*(4), 377–387. http://doi.org/10.1007/s00221-012-3223-4

Dunn, W. (2014). Sensory Profile™ 2. Retrieved from http://www.pearsonclinical.com/therapy/products/100000822/sensory-profile-2.html

Engelhardt, P. E., Ferreira, F., & Patsenko, E. G. (2010). Pupillometry reveals processing load during spoken language comprehension. *Quarterly Journal of Experimental Psychology (2006)*, *63*(4), 639–645. http://doi.org/10.1080/17470210903469864

Erstenyuk, V., Swanson, M. R., & Siller, M. (2014). Pupillary responses during a joint attention task are associated with nonverbal cognitive abilities and sub-clinical symptoms of autism. *Research in Autism Spectrum Disorders*, *8*(6), 644–653. http://doi.org/10.1016/j.rasd.2014.03.003

Falck-Ytter, T. (2008). Face inversion effects in autism: A combined looking time and pupillometric study. *Autism Research*, *1*(5), 297–306. http://doi.org/10.1002/aur.45

Fan, X., Miles, J. H., Takahashi, N., & Yao, G. (2009). Abnormal transient pupillary light reflex in individuals with autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *39*(11), 1499–1508. http://doi.org/10.1007/s10803-009-0767-7

Feldman, R. S., McGee, G. G., Mann, L., & Strain, P. (1993). Nonverbal affective decoding ability in children with autism and in typical preschoolers. *Journal of Early Intervention*, *17*(4), 341–350. http://doi.org/10.1177/105381519301700401

Field, A. (2005). *Discovering Statistics Using SPSS*. London: SAGE Publications. 2455 Teller Road, Thousand Oaks, CA 91320. Tel: 800-818-7243; Tel: 805-499-9774; Fax: 800-583-2665; e-mail: journals@sagepub.com; Web site: http://sagepub.com.

Fitzgerald, H. E. (1968). Autonomic pupillary reflex activity during early infancy and its relation to social and nonsocial visual stimuli. *Journal of Experimental Child Psychology*, *6*(3), 470–482. http://doi.org/10.1016/0022-0965(68)90127-6

Foss-Feig, J. H., Kwakye, L. D., Cascio, C. J., Burnette, C. P., Kadviar, H., Stone, W. L., & Wallace, M. T. (2010). An extended multisensory temporal binding window in autism spectrum disorders. *Experimental Brain Research*, 203 (2), 381 - 389. http://doi.org/10.1007/s00221-010-2240-4

Foxe, J. J., Molholm, S., Bene, V. A. Del, Frey, H.-P., Russo, N. N., Blanco, D., … Ross, L. A. (2013). Severe multisensory speech integration deficits in high-functioning school-aged children with autism spectrum disorder and their resolution during early adolescence. *Cerebral Cortex*, *25*(2), 298–312. http://doi.org/10.1093/cercor/bht213

Gabay, S., Pertzov, Y., & Henik, A. (2011). Orienting of attention, pupil size, and the norepinephrine system. *Attention, Perception & Psychophysics*, *73*(1), 123–129. http://doi.org/10.3758/s13414-010-0015-4

Gelder, B. de, Vroomen, J., & van der Heide, L. (1991). Face recognition and lip-reading in autism. *European Journal of Cognitive Psychology*. http://doi.org/10.1080/09541449108406220

Gingras, B., Marin, M. M., Puig-Waldmüller, E., & Fitch, W. T. (2015). The Eye is Listening: Music-Induced Arousal and Individual Differences Predict Pupillary Responses. *Frontiers in Human Neuroscience*, *9*(November), 619. http://doi.org/10.3389/fnhum.2015.00619

Grandin, T. (1988). Teaching Tips from a Recovered Autistic. *Focus on Autism and Other Developmental Disabilities*. http://doi.org/10.1177/108835768800300101

Granholm, E., Asarnow, R. F., Sarkin, A. J., & Dykes, K. L. (1996). Pupillary responses index cognitive resource limitations. *Psychophysiology*. http://doi.org/10.1111/j.1469-8986.1996.tb01071.x

Grant, K. W., & Seitz, P. F. (2000). The use of visible speech cues for improving auditory detection of spoken sentences. *The Journal of the Acoustical Society of America*, *108*(3 Pt 1), 1197–208. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11008820

Grossman, R. B., Steinhart, E., Mitchell, T., & McIlvane, W. (2015). "Look who's talking!" gaze patterns for implicit and explicit audio-visual speech synchrony detection in children with high-functioning autism. *Autism Research*, *8*(3), 307–316. Retrieved from http://search.proquest.com.ezproxy.library.yorku.ca/psycinfo/docview/1707076864/DF2439A97FCC4E4APQ/1?accountid=15182

Happé, F. (1999). Autism: Cognitive deficit or cognitive style? *Trends in Cognitive Sciences*, *3*(6), 216–222. http://doi.org/10.1016/S1364-6613(99)01318-2

Happé, F., & Frith, U. (2006). The weak coherence account: Detail-focused cognitive style in autism spectrum disorders. *Journal of Autism and Developmental Disorders*. http://doi.org/10.1007/s10803-005-0039-0

Harms, M. B., Martin, A., & Wallace, G. L. (2010). Facial emotion recognition in autism spectrum disorders: A review of behavioral and neuroimaging studies. *Neuropsychology Review*. http://doi.org/10.1007/s11065-010-9138-6

Harrar, V., & Harris, L. R. (2008). The effect of exposure to asynchronous audio, visual, and tactile stimulus combinations on the perception of simultaneity. *Experimental Brain Research*, *186*(4), 517–524. http://doi.org/10.1007/s00221-007-1253-0

Hess, E. H. (1975). *The tell-tale eye: How your eyes reveal hidden thoughts and emotions.* Oxford, England: Van Nostrand Reinhold.

Hillock, A. R., Powers, A. R., & Wallace, M. T. (2011). Binding of sights and sounds: Age-related changes in multisensory temporal processing. *Neuropsychologia*, *49*(3), 461–467. http://doi.org/10.1016/j.neuropsychologia.2010.11.041

Hobson, P., Ouston, J., & Lee, A. (1988). Emotion recognition in autism: Coordinating faces and voices. *Psychological Medicine*, *18*(4), 911–923.

Honey, E., McConachie, H., Turner, M., & Rodgers, J. (2012). Validation of the repetitive behaviour questionnaire for use with children with autism spectrum disorder. *Research in Autism Spectrum Disorders*, *6*(1), 355–364. http://doi.org/10.1016/j.rasd.2011.06.009

Iarocci, G., & McDonald, J. (2006). Sensory integration and the perceptual experience of persons with autism. *Journal of Autism and Developmental Disorders*, *36*(1), 77–90. http://doi.org/10.1007/s10803-005-0044-3

Iarocci, G., Rombough, A., Yager, J., Weeks, D. J., & Chua, R. (2010). Visual influences on speech perception in children with autism. *Autism : The International Journal of Research and Practice*, *14*(4), 305–320. http://doi.org/10.1177/1362361309353615

Irwin, J. R., Tornatore, L. a., Brancazio, L., & Whalen, D. H. (2011). Can children with autism spectrum disorders “hear” a speaking face? *Child Development*, *82*(5), 1397–1403. http://doi.org/10.1111/j.1467-8624.2011.01619.x

Jones, E. J. H., Venema, K., Earl, R., Lowy, R., Barnes, K., Estes, A., … Webb, S. J. (2016). Reduced engagement with social stimuli in 6-month-old infants with later autism spectrum disorder: A longitudinal prospective study of infants at high familial risk. *Journal of*

Neurodevelopmental Disorders, 1–20. http://doi.org/10.1186/s11689-016-9139-8

Jones, R. (1990). Do women and myopes have larger pupils? *Investigative Ophthalmology and Visual Science*, *31*(7), 1413–1415.

Jones, R. S. P., Quigney, C., & Huws, J. C. (2003). First-hand accounts of sensory perceptual experiences in autism: A qualitative analysis. *Journal of Intellectual and Developmental Disability*, *28*(2), 112–121. Retrieved from http://www.tandfonline.com/doi/abs/10.1080/1366825031000147058#.VfnNBp3BzRY

Just, M. A., & Carpenter, P. A. (1993). The intensity dimension of thought: Pupillometric indices of sentence processing. *Canadian Journal of Experimental Psychology*, *47*(2), 310–339.

Kahana-Kalman, R., & Goldman, S. (2008). Intermodal matching of emotional expressions in young children with autism. *Research in Autism Spectrum Disorders*, *2*(2), 301–310. http://doi.org/10.1016/j.rasd.2007.07.004

Kanne, S. M., Randolph, J. K., & Farmer, J. E. (2008). Diagnostic and assessment findings: A bridge to academic planning for children with autism spectrum disorders. *Neuropsychology Review*, *18*(4), 367–384. http://doi.org/10.1007/s11065-008-9072-z

Kanner, L. (1968). Autistic disturbances of affective contact. *Acta Paedopsychiatrica*, *35*(4), 100–136. http://doi.org/10.1105/tpc.11.5.949

Kavšek, M. (2004). Predicting later IQ from infant visual habituation and dishabituation: A meta-analysis. *Journal of Applied Developmental Psychology*. http://doi.org/10.1016/j.appdev.2004.04.006

Klin, A., Jones, W., Schultz, R., Volkmar, F., & Cohen, D. (2011). Visual fixation patterns during viewing of naturalistic social situations as predictors of social competence in individuals with autism. *Archives of General Psychiatry*, *59*(9), 809–816.

Klingner, J., Tversky, B., & Hanrahan, P. (2011). Effects of visual and verbal presentation on cognitive load in vigilance, memory, and arithmetic tasks. *Psychophysiology*, *48*(3), 323–332. http://doi.org/10.1111/j.1469-8986.2010.01069.x

Koelsch, S. (2014). Brain correlates of music-evoked emotions. *Nature Reviews. Neuroscience*, *15*(3), 170–180. http://doi.org/10.1038/nrn3666

Kuchinke, L., Schneider, D., Kotz, S. a., & Jacobs, A. M. (2011). Spontaneous but not explicit processing of positive sentences impaired in Asperger's syndrome: Pupillometric evidence. *Neuropsychologia*, *49*(3), 331–338. http://doi.org/10.1016/j.neuropsychologia.2010.12.026

Kuhl, P. K., & Meltzoff, A. N. (1984). The intermodal representation of speech in infants. *Infant Behavior and Development*. http://doi.org/10.1016/S0163-6383(84)80050-8

Kwakye, L. D., Foss-Feig, J. H., Cascio, C. J., Stone, W. L., & Wallace, M. T. (2011a). Altered auditory and multisensory temporal processing in autism spectrum disorders. *Frontiers in Integrative Neuroscience*, *4*(January), 129. http://doi.org/10.3389/fnint.2010.00129

Kwakye, L. D., Foss-Feig, J. H., Cascio, C. J., Stone, W. L., & Wallace, M. T. (2011b). Altered auditory and multisensory temporal processing in autism spectrum disorders. *Frontiers in Integrative Neuroscience*, *4*, 129. http://doi.org/10.3389/fnint.2010.00129

Leekam, S., Tandos, J., McConachie, H., Meins, E., Parkinson, K., Wright, C., … Couteur, A. Le. (2007). Repetitive behaviours in typically developing 2-year-olds. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *48*(11), 1131–1138. http://doi.org/10.1111/j.1469-7610.2007.01778.x

Lenroot, R. K., & Yeung, P. K. (2013). Heterogeneity within autism spectrum disorders: What have we learned from neuroimaging studies? *Frontiers in Human Neuroscience*, *7*(October), 733. http://doi.org/10.3389/fnhum.2013.00733

Lewkowicz, D. J. (2010). Infant perception of audio-visual speech synchrony. *Developmental Psychology*, *46*(1), 66–77. http://doi.org/10.1037/a0015579

Libby, W. L., Lacey, B. C., & Lacey, J. I. (1973). Pupillary and cardiac activity during visual attention. *Psychophysiology*, *10*(3), 270–294. http://doi.org/10.1111/j.1469-8986.1973.tb00526.x

Lidstone, J., Uljarević, M., Sullivan, J., Rodgers, J., McConachie, H., Freeston, M., … Leekam, S. (2014). Relations among restricted and repetitive behaviors, anxiety and sensory features in children with autism spectrum disorders. *Research in Autism Spectrum Disorders*, *8*(2), 82–92. http://doi.org/10.1016/j.rasd.2013.10.001

Lord, C., Rutter, M., DiLavore, P. C., Risi, S., Gotham, K., & Bishop, S. (2012). Autism diagnostic observation schedule, second edition. *Torrance, CA: Western Psychological Services.* Retrieved from https://www.google.ca/search?q=Lord%2C+C.%2C+Rutter%2C+M.%2C+DiLavore%2C+P.+C.%2C+Risi%2C+S.%2C+Gotham%2C+K.%2C+%26+Bishop%2C+S.+(2012).+Autism+diagnostic+observation+schedule%2C+second+edition.+Torrance%2C+CA%3A+Western+Psychological+Services.&oq=Lord%2C

Lord, C., Risi, S., Lambrecht, L., Cook, E. H., Leventhal, B. L., Dilavore, P. C., … Rutter, M. (2000). The Autism Diagnostic Observation Schedule-Generic: A standard measure of social and communication deficits associated with the spectrum of autism. *Journal of Autism and Developmental Disorders*, *30*(3), 205–223. http://doi.org/10.1023/A:1005592401947

Loveland, K., Tunali-Kotoski, B., Chen, Y., Pearson, D., Brelsfors, K., & Gibbs, M. (1997). Emotion recognition in autism: Verbal and nonverbal information. *Development and Psychopathology*, *9*(3), 579–593. http://doi.org/10.1017/S0954579497001351

MacDonald, J., & McGurk, H. (1978). Visual influences on speech perception processes. *Perception & Psychophysics*, *24*(3), 253–257. http://doi.org/10.3758/BF03206096

MacLachlan, C., & Howland, H. C. (2002). Normal values and standard deviations for pupil diameter and interpupillary distance in subjects aged 1 month to 19 years. *Ophthalmic and Physiological Optics*, *22*(3), 175–182. http://doi.org/10.1046/j.1475-1313.2002.00023.x

Martineau, J., Hernandez, N., Hiebel, L., Roché, L., Metzger, A., & Bonnet-Brilhault, F. (2011). Can pupil size and pupil responses during visual scanning contribute to the diagnosis of autism spectrum disorder in children? *Journal of Psychiatric Research*, *45*(8), 1077–1082. http://doi.org/10.1016/j.jpsychires.2011.01.008

McCrimmon, a., & Rostad, K. (2013). Test Review: Autism Diagnostic Observation Schedule, Second Edition (ADOS-2) Manual (Part II): Toddler Module. *Journal of Psychoeducational Assessment*, *32*(1), 88–92. http://doi.org/10.1177/0734282913490916

Menard, S. (1995). *Applied Logistic Regression Analysis. Sage university paper series on quantitative applications in the social sciences.* Thousand Oaks, CA.: SAGE Publications. 2455 Teller Road, Thousand Oaks, CA 91320. Tel: 800-818-7243; Tel: 805-499-9774; Fax: 800-583-2665; e-mail: journals@sagepub.com; Web site: http://sagepub.com.

Mendelson, M. J., & Ferland, M. B. (1982). Auditory-visual transfer in four-month-old infants. *Child Development*, *53*(4), 1022–1027. http://doi.org/10.2307/1129143

Mongillo, E. a., Irwin, J. R., Whalen, D. H., Klaiman, C., Carter, A. S., & Schultz, R. T. (2008).

Audiovisual processing in children with and without autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *38*(7), 1349–1358. http://doi.org/10.1007/s10803-007-0521-y

Monk, C. S., Weng, S.-J., Wiggins, J. L., Kurapati, N., Louro, H. M. C., Carrasco, M., … Lord, C. (2010). Neural circuitry of emotional face processing in autism spectrum disorders. *Journal of Psychiatry & Neuroscience : JPN*, *35*(2), 105–114. http://doi.org/10.1503/jpn.090085

Myers, R. (1990). *Classical and modern regression with applications.* (2nd ed.). Boston. MA.: Duxbury.

Nakano, T., Tanaka, K., Endo, Y., Yamane, Y., Yamamoto, T., Nakano, Y., … Kitazawa, S. (2010). Atypical gaze patterns in children and adults with autism spectrum disorders dissociated from developmental changes in gaze behaviour. *Proceedings. Biological Sciences / The Royal Society*, *277*(1696), 2935–2943. http://doi.org/10.1098/rspb.2010.0587

Navarra, J., Vatakis, A., Zampini, M., Soto-Faraco, S., Humphreys, W., & Spence, C. (2005). Exposure to asynchronous audiovisual speech extends the temporal window for audiovisual integration. *Cognitive Brain Research*, *25*(2), 499–507. http://doi.org/10.1016/j.cogbrainres.2005.07.009

Nuske, H. J., Vivanti, G., & Dissanayake, C. (2014a). Brief Report: Evidence for Normative Resting-State Physiology in Autism. *Journal of Autism and Developmental Disorders*, *44*(8), 2057–2063. http://doi.org/10.1007/s10803-014-2068-z

Nuske, H. J., Vivanti, G., & Dissanayake, C. (2014b). Reactivity to fearful expressions of familiar and unfamiliar people in children with autism: an eye-tracking pupillometry study.

Journal of Neurodevelopmental Disorders, *6*(1), 14. http://doi.org/10.1186/1866-1955-6-14

Nuske, H. J., Vivanti, G., & Dissanayake, C. (2015). No evidence of emotional dysregulation or aversion to mutual gaze in preschoolers with autism spectrum disorder: An eye-tracking pupillometry study. *Journal of Autism and Developmental Disorders*, *45*(11), 3433–3445. http://doi.org/10.1007/s10803-015-2479-5

Nyström, P., Gredebäck, G., Bölte, S., & Falck-Ytter, T. (2015). Hypersensitive pupillary light reflex in infants at risk for autism. *Molecular Autism*, *6*, 10. http://doi.org/10.1186/s13229-015-0011-6

Oka, S., Chapman, C. R., & Jacobson, R. C. (2000). Phasic pupil dilation response to noxious stimulation: Effects of conduction distance, sex, and age. *Journal of Psychophysiology*, *14*(2), 97–105.

Osterling, J., & Dawson, G. (1994). Early recognition of children with autism: A study of first birthday home videotapes. *Journal of Autism and Developmental Disorders*, *24*(3), 247–257. http://doi.org/10.1007/BF02172225

Ozonoff, S., Pennington, B. F., & Rogers, S. J. (1990). Are there emotion perception deficits in young autistic children? *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *31*(3), 343–361. http://doi.org/10.1111/j.1469-7610.1990.tb01574.x

Panksepp, J., & Bernatzky, G. (2002). Emotional sounds and the brain: The neuro-affective foundations of musical appreciation. *Behavioural Processes*, *60*(2), 133–155. http://doi.org/10.1016/S0376-6357(02)00080-3

Partala, T., Jokiniemi, M., & Surakka, V. (2000). Pupillary responses to emotionally provocative stimuli. In *Proceedings of the symposium on Eye tracking research & applications - ETRA*

’00 (pp. 123–129). New York, New York, USA: ACM Press. http://doi.org/10.1145/355017.355042

Pierce, K., Conant, D., Hazin, R., Stoner, R., & Desmond, J. (2011). Preference for geometric patterns early in life as a risk factor for autism. *Archives of General Psychiatry*, *68*(1), 101–109. http://doi.org/10.1001/archgenpsychiatry.2010.113

Pierce, K., & Redcay, E. (2008). Fusiform function in children with an autism spectrum disorder is a matter of “who.” *Biological Psychiatry*, *64*(7), 552–560. http://doi.org/10.1016/j.biopsych.2008.05.013

Pohar, M., Blas, M., & Turk, S. (2004). Comparison of Logistic Regression and Linear Discriminant Analysis : A Simulation Study. *Advances in Methodology and Statistics*, *1*(1), 143–161.

Porter, G., Troscianko, T., & Gilchrist, I. D. (2007). Effort during visual search and counting: insights from pupillometry. *Quarterly Journal of Experimental Psychology (2006)*, *60*(2), 211–29. http://doi.org/10.1080/17470210600673818

Riby, D. M., & Hancock, P. J. B. (2008). Viewing it differently: Social scene perception in Williams syndrome and Autism. *Neuropsychologia*, *46*(11), 2855–2860. http://doi.org/10.1016/j.neuropsychologia.2008.05.003

Rieffe, C., Ketelaar, L., & Wiefferink, C. H. (2010). Assessing empathy in young children: Construction and validation of an Empathy Questionnaire (EmQue). *Personality and Individual Differences*, *49*(5), 362–367. http://doi.org/10.1016/j.paid.2010.03.046

Robel, L., Ennouri, K., Piana, H., Vaivre-Douret, L., Perier, A., Flament, M. F., & Mouren-Siméoni, M. C. (2004). Discrimination of face identities and expressions in children with autism: Same or different? *European Child and Adolescent Psychiatry*, *13*(4), 227–233. http://doi.org/10.1007/s00787-004-0409-8

Rosset, D. B., Rondan, C., Da Fonseca, D., Santos, A., Assouline, B., & Deruelle, C. (2008). Typical emotion processing for cartoon but not for real faces in children with autistic spectrum disorders. *Journal of Autism and Developmental Disorders*, *38*(5), 919–925. http://doi.org/10.1007/s10803-007-0465-2

Rubin, L. S. (1961). Patterns of pupillary dilatation and constriction in psychotic adults and autistic children. *The Journal of Nervous and Mental Disease*. http://doi.org/10.1097/00005053-196108000-00009

Rutter Bailey, A., & Lord, C., M. (2003). *Social Communication Questionnaire*. *Los Angeles, CA*.

Schopler, E., Reichler, R. J., DeVellis, R. F., & Daly, K. (1980). Toward objective classification of childhood autism: Childhood Autism Rating Scale (CARS). - PsycINFO - ProQuest. *Journal of Autism and Developmental Disorders*, *10*(1), 91–103. Retrieved from http://search.proquest.com.ezproxy.library.yorku.ca/psycinfo/docview/616418532/5B76740781CB4F49PQ/1?accountid=15182

Segers, M., & Bebko, J. M. (2012). A Dynamic Aproach to Temporal Binding in Audiovisual Integration. (Unpublished master's thesis). York University, Toronto, Canada.

Senju, A., Southgate, V., White, S., & Frith, U. (2009). Mindblind eyes: An absence of spontaneous theory of mind in Asperger syndrome. (1). *Science (New York, N.Y.)*, *325*(5942), 883–885. http://doi.org/10.1126/science.1176170

Sepeta, L., Tsuchiya, N., Davies, M. S., Sigman, M., Bookheimer, S. Y., & Dapretto, M. (2012).

Abnormal social reward processing in autism as indexed by pupillary responses to happy faces. *Journal of Neurodevelopmental Disorders*, *4*(17), 1–9.

Sigman, M., Cohen, S. E., & Beckwith, L. (1997). Why does infant attention predict adolescent intelligence? *Infant Behavior and Development*. http://doi.org/10.1016/S0163-6383(97)90016-3

Sigman, M., Dijamco, A., Gratier, M., & Rozga, A. (2004). Early detection of core deficits in autism. *Mental Retardation and Developmental Disabilities Research Reviews*. http://doi.org/10.1002/mrdd.20046

Silk, J. S., Dahl, R. E., Ryan, N. D., Forbes, E. E., & Axelson, D. a. (2007). Pupillary reactivity to emotional information in child and adolescent depression: Links to clinical and ecological measures. *The American Journal of Psychiatry*, *164*(12), 1873–1880.

Skuse, D. H., Mandy, W. P. L., & Scourfield, J. (2005). Measuring autistic traits: Heritability, reliability and validity of the Social and Communication Disorders Checklist. *British Journal of Psychiatry*, *187*(DEC.), 568–572. http://doi.org/10.1192/bjp.187.6.568

Smith, E. G., & Bennetto, L. (2007). Audiovisual speech integration and lipreading in autism. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *48*(8), 813–821. http://doi.org/10.1111/j.1469-7610.2007.01766.x

South, M., Ozonoff, S., & McMahon, W. M. (2005). Repetitive behavior profiles in asperger syndrome and high-functioning autism. *Journal of Autism and Developmental Disorders*, *35*(2), 145–158. http://doi.org/10.1007/s10803-004-1992-8

Stanners, R. F., Coulter, M., Sweet, A. W., & Murphy, P. (1979). The pupillary response as an indicator of arousal and cognition. *Motivation and Emotion*, *3*(4), 319–340.

http://doi.org/10.1007/BF00994048

Steinhauer, S. R., & Hakerem, G. (1992). The pupillary response in cognitive psychophysiology and schizophrenia. *Annals of the New York Academy of Sciences*, *658*, 182–204. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/1497258

Stern, R. M., Ray, W. J., & Quigley, K. S. (2001). Psychophysiological Recording (2nd Editio, pp. 125–141). New York: Oxford University Press. Retrieved from https://books.google.ca/books/about/Psychophysiological_Recording.html?id=9WmvzrkZdv8C&pgis=1

Stevenson, R. A., Segers, M., Ferber, S., Barense, M. D., Camarata, S., & Wallace, M. T. (2015). Keeping time in the brain: Autism spectrum disorder and audiovisual temporal processing. *Autism Research*, *9*(7), 720–738. http://doi.org/10.1002/aur.1566

Stevenson, R. A., Siemann, J. K., Woynaroski, T. G., Schneider, B. C., Eberly, H. E., Camarata, S. M., & Wallace, M. T. (2014a). Evidence for Diminished Multisensory Integration in Autism Spectrum Disorders. *Journal of Autism and Developmental Disorders*, *44*(12). http://doi.org/10.1007/s10803-014-2179-6

Stevenson, R. A., Segers, M., Ferber, S., Barense, M. D., & Wallace, M. T. (2014b). The impact of multisensory integration deficits on speech perception in children with autism spectrum disorders. *Frontiers in Psychology*, *5*, 379. http://doi.org/10.3389/fpsyg.2014.00379

Stevenson, R. A., Zemtsov, R. K., & Wallace, M. T. (2012a). Individual differences in the multisensory temporal binding window predict susceptibility to audiovisual illusions. *Journal of Experimental Psychology: Human Perception and Performance*. http://doi.org/10.1037/a0027339

Stevenson, R. A, Siemann, J. K., Schneider, B. C., Eberly, H. E., Woynaroski, T. G., Camarata, S. M., & Wallace, M. T. (2014c). Multisensory temporal integration in autism spectrum disorders. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *34*(3), 691–7. http://doi.org/10.1523/JNEUROSCI.3615-13.2014

Sumby, W. H., & Pollack, I. (1954). Visual Contribution to Speech Intelligibility in Noise. *The Journal of the Acoustical Society of America*. http://doi.org/10.1121/1.1907309

Tomchek, S. D., & Dunn, W. (2007). Sensory processing in children with and without autism: a comparative study using the short sensory profile. *The American Journal of Occupational Therapy. : Official Publication of the American Occupational Therapy Association*, *61*(2), 190–200. http://doi.org/10.5014/ajot.61.2.190

Turner, M. (1996). Repetitive behaviour and cognitive functioning in autism. Unpublished PhD, University of Cambridge.

van der Meer, R., Beyer, R., Horn, J., Foth, M., Bornemann, B., Ries, J., … Wartenburger, I. (2010). Resource allocation and fluid intelligence: Insights from pupillometry. *Psychophysiology*, *47*, 158–169. http://doi.org/10.1111/j.1469-8986.2009.00884.x

Van Engeland, H., Roelofs, J. W., Verbaten, M. N., & Slangen, J. L. (1991). Abnormal electrodermal reactivity to novel visual stimuli in autistic children. *Psychiatry Research*, *38*(1), 27–38. http://doi.org/10.1016/0165-1781(91)90050-Y

Van Gerven, P. W. M., Paas, F., Van Merriënboer, J. J. G., & Schmidt, H. G. (2004). Memory load and the cognitive pupillary response in aging. http://doi.org/10.1111/j.1469-8986.2003.00148.x

Wagner, J. B., Hirsch, S. B., Vogel-Farley, V. K., Redcay, E., & Nelson, C. A. (2013). Eye-tracking, autonomic, and electrophysiological correlates of emotional face processing in adolescents with autism spectrum disorder. *Journal of Autism and Developmental Disorders*. 43, 188-199. http://doi.org/10.1007/s10803-012-1565-1

Wang, A. T., Lee, S. S., Sigman, M., & Dapretto, M. (2007). Reading affect in the face and voice. *Archives of General Psychiatry*, *64*(June), 698–708. http://doi.org/10.1001/archpsyc.64.6.698

Wechsler, D. (2011). Wechsler Abbreviated Scale of Intelligence® - Second Edition. Retrieved from http://www.pearsonclinical.com/psychology/products/100000037/wechsler-abbreviated-scale-of-intelligence--second-edition-wasi-ii.html

Whitehouse, A. J. O., & Bishop, D. V. M. (2008). Do children with autism "switch off" to speech sounds? An investigation using event-related potentials. *Developmental Science*, *11*(4), 516–524. http://doi.org/10.1111/j.1467-7687.2008.00697.x

Williams, D. L., Goldstein, G., & Minshew, N. J. (2005). Impaired memory for faces and social scenes in autism: Clinical implications of memory dysfunction. *Archives of Clinical Neuropsychology*, *20*(1), 1–15. http://doi.org/10.1016/j.acn.2002.08.001

Williams, J. H. G., Massaro, D. W., Peel, N. J., Bosseler, A., & Suddendorf, T. (2004). Visual-auditory integration during speech imitation in autism. *Research in Developmental Disabilities*, *25*(6), 559–575. http://doi.org/10.1016/j.ridd.2004.01.008

Wing, L., Leekam, S. R., Libby, S. J., Gould, J., & Larcombe, M. (2002). The Diagnostic Interview for Social and Communication Disorders: Background, inter-rater reliability and clinical use. *Journal of Child Psychology and Psychiatry*, *43*(3), 307–25. http://doi.org/10.1111/1469-7610.00023

Winn, B., Whitaker, D., Elliott, D. B., & Phillips, N. J. (1994). Factors affecting light-adapted pupil size in normal human subjects. *Investigative Ophthalmology & Visual Science*, *35*(3), 1132–7. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/8125724

Woynaroski, T. G., Kwakye, L. D., Foss-Feig, J. H., Stevenson, R. a., Stone, W. L., & Wallace, M. T. (2013). Multisensory speech perception in children with autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *43*(12), 2891–2902. http://doi.org/10.1007/s10803-013-1836-5

Zandt, F., Prior, M., & Kyrios, M. (2007). Repetitive behaviour in children with high functioning autism and obsessive compulsive disorder. *Journal of Autism and Developmental Disorders*, *37*(2), 251–259. http://doi.org/10.1007/s10803-006-0158-2

Appendices

Appendix A: Assumptions of General Linear Model

Normality Assessment of Outcome Variables

	Normality Indicators			Homogeneity of Variance Indicator
Variable	Skewness Z-value	Kurtosis Z-value	Shapiro-Wilk Sig. Value	Levene's Test Sig. Value
Social Linguistic_Sync	1.66	1.52	.081	.180
Social Linguistic_AV	1.71	.61	.232	.133
Social Linguistic_VA	.38	-.10	.498	**.040**
Social Non-Linguistic_Sync	1.48	.92	.303	.435
Social Non-Linguistic_AV	-.41	.13	.871	.520
Social Non-Linguistic_VA	**2.25**	-.45	**.001**	.792
Social Emotional Happy_ Sync	**3.46**	**3.34**	**.005**	.474
Social Emotional Happy_ AV	1.17	.45	.135	.147
Social Emotional Happy_ VA	1.16	.60	.602	.530
Social Emotional Sad_ Sync	-.49	1.13	.466	.476
Social Emotional Sad_ AV	1.46	-.12	.259	.080
Social Emotional Sad_ VA	**3.12**	**2.53**	**.006**	.219
Non Social Non-Linguistic_Sync	**3.63**	**6.18**	**.002**	.391
Non Social Non-Linguistic_AV	.33	-.61	.828	.049
Non Social Non-Linguistic_VA	**2.25**	.45	.007	.318

* Bolded values exceed cut-off

Appendix B: Descriptive Statistics for Pupillary Responses to Conditions

Descriptive Statistics for Change from Interstimulus Trial for Each Condition		
Total N = 71	**ASD (Total N = 39)**	**TD (Total N = 32)**
	M (SD)	
Social Linguistic		
Synchronous	.095 (.120)	.159 (.134)
Audio-Leading	.111 (.132)	.194 (.097)
Visual-Leading	.102 (.143)	.161 (.110)
Social Non-Linguistic		
Synchronous	.082 (.133)	.153 (.135)
Audio-Leading	.099 (.140)	.186 (.124)
Visual-Leading	.083 (.141)	.159 (.136)
Social – Emotional		
Synchronous	.122 (.153)	.199 (.143)
Audio-Leading	.091 (.133)	.148 (.093)
Visual-Leading	.106 (.141)	.148 (.115)
Non-Social Non-Linguistic		
Synchronous	.154 (.227)	.178 (.173)
Audio-Leading	.174 (.185)	.202 (.131)
Visual-Leading	.122 (.162)	.156 (.142)

Appendix C: Correlations Between Pupillary Responses and ASD Symptoms

Table C1.
Pearson Correlations between Synchronous Social Conditions and the Autism Spectrum Questionnaire - Child

	Total Score	Social Skills	Attention Switching	Attention to Detail	Communication	Imagination
ASD (N = 38)						
Social-Linguistic	-0.02	0.132	0.074	0.039	-0.192	-0.12
Social Non-Linguistic	-0.198	0.086	-0.164	-0.212	-0.089	-0.227
Social-Emotional	-0.209	-0.114	-0.177	0.077	-0.242	-0.268
TD (N = 32)	**Total Score**	**Social Skills**	**Attention Switching**	**Attention to Detail**	**Communication**	**Imagination**
Social-Linguistic	0.061	0.114	0.046	-0.058	0.099	-0.013
Social Non-Linguistic	0.18	0.079	0.134	0.017	0.258	0.104
Social-Emotional	0.214	0.032	0.138	0.097	0.339	0.1

Note: There were no significant correlations at $p < .05$ (2-tailed).

Table C2.
Pearson Correlations between Synchronous Social Conditions and the Social Responsiveness Scale

	Total Score	Social Awareness	Social Cognition	Social Communication	Social Motivation	RRB	SCI
ASD (N = 38)							
Social-Linguistic	-0.113	-0.11	-0.106	-0.021	0.062	**-.366***	-0.039
Social Non-Linguistic	-0.178	-0.088	-0.207	-0.068	-0.097	**-.356***	-0.122
Social-Emotional	-0.31	**-.340***	-0.286	-0.201	-0.151	**-.461****	-0.254
TD (N = 32)	**Total Score**	**Social Awareness**	**Social Cognition**	**Social Communication**	**Social Motivation**	**RRB**	**SCI**
Social-Linguistic	0.143	0.11	0.103	0.146	0.084	0.161	0.132
Social Non-Linguistic	0.274	0.216	0.143	0.249	0.287	0.298	0.258
Social-Emotional	0.338	**.377***	0.236	0.348	0.261	0.281	0.344

* Correlation is significant at $p < .05$ (2-tailed). ** Correlation is significant at $p < .01$ (2-tailed).

Table C3.
Pearson Correlations between Synchronous Social Conditions and the Repetitive Behaviour Questionnaire

ASD (N = 39)							
	Total Score	**Factor 1**	**Factor 2**	**Factor 3**	**Factor 4**	**Motor Sensory**	**Rigidity Routines**
Social-Linguistic	-0.31	-0.307	-0.295	-0.266	-0.207	-0.291	-0.313
Social Non-Linguistic	-0.291	-0.195	-0.245	-0.298	-0.305	-0.252	-0.269
Social-Emotional	-0.304	-0.295	-0.229	-0.305	-0.15	-0.286	-0.277
TD (N = 32)							
	Total Score	**Factor 1**	**Factor 2**	**Factor 3**	**Factor 4**	**Motor Sensory**	**Rigidity Routines**
Social-Linguistic	-0.18	0.019	-0.283	-0.134	-0.082	-0.023	-0.27
Social Non-Linguistic	0.129	0.094	0.103	0.128	0.221	0.14	0.077
Social-Emotional	-0.012	-0.038	0.069	-0.04	0.146	-0.008	0.038

Note: There were no significant correlations at $p < .05$ (2-tailed).

Table C4.
Pearson Correlations between Asynchronous Conditions and the Autism Spectrum Questionnaire - Child

ASD (N = 38)						
	Total Score	**Social Skills**	**Attention Switching**	**Attention to Detail**	**Communication**	**Imagination**
Social-Linguistic	-0.138	0.158	0.037	0.016	**-.349***	-0.312
Social Non-Linguistic	-0.28	0.025	-0.058	-0.125	**-.425****	-0.305
Social-Emotional	-0.24	-0.016	-0.16	0.074	**-.415****	-0.304
Non-Social Non-Linguistic	-0.039	0.087	-0.134	0.218	-0.235	-0.134
TD (N = 32)						
	Total Score	**Social Skills**	**Attention Switching**	**Attention to Detail**	**Communication**	**Imagination**
Social-Linguistic	0.179	0.073	0.084	0.124	0.292	-0.004
Social Non-Linguistic	0.088	-0.059	0.052	0.154	0.092	0.056
Social-Emotional	0.284	0.088	0.249	0.186	0.296	0.113
Non-Social Non-Linguistic	**.423***	0.15	**.455****	0.119	**.400***	0.289

Note: There were no significant correlations at $p < .05$ (2-tailed).

Table C5.
Pearson Correlations between Asynchronous Conditions and the Social Responsiveness Scale

ASD (N = 38)							
	Total Score	**Social Awareness**	**Social Cognition**	**Social Communication**	**Social Motivation**	**RRB**	**SCI**
Social-Linguistic	-0.187	-0.277	-0.158	-0.154	0.047	**-0.32***	-0.141
Social Non-Linguistic	-0.289	-0.225	-0.28	-0.257	-0.02	**-.470****	-0.226
Social-Emotional	**-.342***	**-.336***	**-.346***	-0.259	-0.101	**-.502****	-0.282
Non-Social Non-Linguistic	-0.127	-0.138	-0.159	-0.078	0.052	-0.261	-0.085
TD (N = 32)							
	Total Score	**Social Awareness**	**Social Cognition**	**Social Communication**	**Social Motivation**	**RRB**	**SCI**
Social-Linguistic	0.293	0.298	0.156	0.293	0.287	0.266	0.293
Social Non-Linguistic	0.152	0.152	0.078	0.139	0.223	0.097	0.164
Social-Emotional	0.273	0.305	0.207	0.271	0.29	0.163	0.299
Non-Social Non-Linguistic	**.486****	**.554****	**.384***	**.453****	**.438***	**.378***	**.504****

* Correlation is significant at $p < .05$ (2-tailed). ** Correlation is significant at $p < .01$ (2-tailed).

Table C6.
Pearson Correlations between Asynchronous Conditions and the Repetitive Behaviour Questionnaire

	Total Score	Factor 1	Factor 2	Factor 3	Factor 4	Motor Sensory	Rigidity Routines
ASD (N = 39)							
Social-Linguistic	-0.155	-0.276	-0.084	-0.095	-0.034	-0.225	-0.109
Social Non-Linguistic	-0.293	-0.268	-0.224	-0.307	-0.13	-0.292	-0.251
Social-Emotional	-0.254	-0.256	-0.189	-0.251	-0.119	-0.239	-0.239
Non-Social Non-Linguistic	-0.216	-0.111	-0.224	-0.222	-0.174	-0.120	-0.250
TD (N = 32)							
	Total Score	**Factor 1**	**Factor 2**	**Factor 3**	**Factor 4**	**Motor Sensory**	**Rigidity Routines**
Social-Linguistic	-0.023	0.066	-0.008	-0.080	0.039	0.063	-0.054
Social Non-Linguistic	-0.097	-0.134	0.016	-0.090	0.042	-0.083	-0.019
Social-Emotional	-0.094	-0.013	-0.027	-0.157	0.025	-0.005	-0.086
Non-Social Non-Linguistic	0.181	0.249	0.132	0.009	0.276	0.258	0.119

Note: There were no significant correlations at $p < .05$ (2-tailed).

Table C7.

Pearson Correlations between Conditions and the Child Sensory Profile for ASD Participants.

Total N = 38	**SL**	**SNL**	**SE**	**NSNL**
SP Total Score	-.301	**-.448****	**-.354***	-.259
SP Quadrant Subscales				
Seeking/Seeker	**-.394***	**-.477****	**-.420****	-.299
Avoiding/Avoider	-.236	**-.395***	**-.379***	-.203
Sensitivity/Sensor	-.187	**-.345***	-.168	-.219
Registration/Bystander	-.305	**-.394***	**-.363***	-.195
SP Sensory Subscales				
Auditory	-.005	-.152	-.089	-.029
Visual	-.083	-.180	-.068	-.107
Touch	-.272	**-.325***	**-.320***	-.213
Movement	**-.523****	**-.525****	**-.485****	-.251
Body Position	-.098	-.164	-.065	-.068
Oral	-.225	**-.442****	-.201	**-.426****
SP Behavioural Subscales				
Conduct	-.386	**-.513****	**-.474****	-.265
Social Emotional	-.189	-.298	**-.362***	-.183
Attentional	**-.346***	**-.414****	**-.394***	-.155

* Correlation is significant at $p < .05$ (2-tailed). ** Correlation is significant at $p < .01$ (2-tailed). SL = Social Linguistic, SNL = Social Non-Linguistic, SE = Social-Emotional, NSNL = Non-Social Non-Linguistic; Synchronous and asynchronous conditions combined.