Contents

Preface \hspace{0.5cm} vii
List of Figures \hspace{0.5cm} xi
List of Tables \hspace{0.5cm} xxi

1 Distorted Multisensory Experiences of Order and Simultaneity \hspace{0.5cm} 1
   Argiro Vatakis and Alexandra Elissavet Bakou

2 Abnormal Timing and Time Perception in Autism Spectrum Disorder?
   A Review of the Evidence \hspace{0.5cm} 37
   Melissa J. Allman and Christine M. Falter

3 A Social Timing Model of Autism, Informed by Typical Development \hspace{0.5cm} 57
   Dawn Wimpory

4 Time Processing in Schizophrenia \hspace{0.5cm} 93
   Deana B. Davalos and Jamie Opper

5 Sense of Time Continuity: Possible Mechanisms of Disruption in
   Schizophrenia \hspace{0.5cm} 115
   Anne Giersch, Laurence Lalanne, Mitsouko van Assche, Patrick E.
   Poncelet, and Mark A. Elliott

6 Predictive Timing for Rhythmic Motor Actions in Schizophrenia \hspace{0.5cm} 136
   Yvonne Delevoye-Turrell, Hélène Wilquin, and Mariama Dione

7 Interactions of Timing and Motivational Impairments in
   Schizophrenia \hspace{0.5cm} 168
   Ryan D. Ward, Billur Avlar, and Peter D. Balsam

8 Timing in Neurogenerative Disorders of the Basal Ganglia \hspace{0.5cm} 190
   Deborah L. Harrington and Stephen M. Rao

9 Timing in the Cerebellum and Cerebellar Disorders \hspace{0.5cm} 226
   Rebecca M. C. Spencer
10  Striatal and Frontal Pathology: Parkinson's Disease and Patients with Lesions of the Basal Ganglia and Frontal Cortex  250
    Catherine R.G. Jones and Marjan Jahanshahi

11  Bayesian Models of Interval Timing and Distortions in Temporal Memory as a Function of Parkinson's Disease and Dopamine-Related Error Processing  281
    Bon-Mi Gu, Anita J. Jurkowski, Jessica I. Lake, Chara Malapani, and Warren H. Meck

12  Aphasia as a Temporal Information Processing Disorder  328
    Elzbieta Szelag, Aneta Szymaszek and Anna Oron

13  How Could Circadian Clock Genes influence Short Duration Timing?  356
    Brad Nicholas

Index  383
CHAPTER 1

Distorted Multisensory Experiences of Order and Simultaneity

Argiro Vatakis* and Alexandra Elissavet Bakou**

1 Introduction

In order to deal appropriately with the events in its environment, an animal must perform at least two essential actions. It must be able to identify or characterize an event, and it must also be able to determine when the particular event occurred in relation to other events. […] “Meaning” requires that the unitary bits of information be kept in a proper sequence.

Efron, 1963a

In his 1963a paper, Efron points out the importance of event identification and event ordering for the construction of meaning. Given that we live and thrive in a multisensory environment, Efron’s ‘unitary bits’ include information from multiple sensory modalities that may be complementary, contradictory or at some level of equivalence. The percept of these sensory ‘bits’ of information as synchronous and unified leads to the percept of a multisensory event rather than multiple, independent sensory events (Vatakis & Spence, 2010). Research to date has shown that the human perceptual system maintains the percept of synchrony between two sensory streams even though these streams may be processed/presented close but not exactly in time (Vatakis, 2013). The maintenance of a synchronous percept is accomplished through the hypothesized existence of a temporal window of integration (TWI; i.e., the interval in which no signal discrepancy is perceived, anything beyond this interval will normally be perceived as being desynchronized or asynchronous; e.g., King, 2005; Spence & Squire, 2003; Vatakis & Spence, 2010; Vroomen & Keetels, 2010). We, thus, have ‘moments’ (or ‘functional moments’ as per Wittmann, 2011) that have no perceivable duration and can be perceived as simultaneous or ‘somewhat’ simultaneous (yet order cannot be perceived) and ‘moments’ that are successive with specific and detectable order of presentation (e.g., Pöppel, 1985, 2004;
Wittmann, 2011). These ‘moments’ are integrated into ‘event intervals’ (or ‘experienced moments’; Wittmann, 2011) that compose our percept of a continuously flowing multisensory event. But how these ‘moments’ and ‘intervals’ associate/interact so as to provide the continuously flowing in time experience of multisensory events?

The majority of clinical research in timing has focused on the ‘event interval’ level (e.g., Allman, 2011; Buhusi & Meck, 2005), while multisensory ‘moments’ and their integration have been understudied, thus, ignoring the potential link of the experience of intervals according to the synchrony and unity of moments. For example, it may be the case that high pacemaker rates may be associated with higher temporal resolution of the timing mechanism(s), which, in turn, should result in lower temporal discrimination thresholds (i.e., better performance and, thus, smaller TWIs; Rammsayer & Classen, 1997; Wenke & Haggard, 2009). Such associations have not been attempted partially due to that fact that researchers in the two areas of focus – synchrony perception and interval timing – have been working in isolation, but also because the mechanisms governing the integration of multisensory moments to event intervals have not been elucidated. Given, therefore, the previous focus on interval timing in clinical populations, in this chapter we will review the literature on multisensory temporal processing in various disorders/conditions in an attempt to draw some first conclusions and encourage future research on the association of multisensory temporal integration, interval timing, and event perception.

2        Multisensory Temporal Integration: A First Look

Our everyday and effortless (as it seems) experience of multisensory events, which are temporally and semantically unified, allows for faster and more accurate detection, discrimination, and localization of targets at hand. Thus, the multisensorial nature of our experiences, not only makes life more enjoyable, but also provides valuable behavioral and perceptual benefits (Calvert, Spence, & Stein, 2004). These benefits along with the altered percepts that are born out of crossmodal interactions (e.g., the McGurk effect, the visual influence on the perception of audiovisual speech; MacDonald & McGurk, 1978) have lead to a vigorous body of research on multisensory processing during the last 20–30 years. Given the ‘young age’ of this area, multisensory temporal integration have primarily been investigated in healthy participants, while the majority of studies with patients experiencing a disruption of audiovisual perception could potentially be interpreted as a consequence of other neurological deficits (e.g., Böhning, Campbell, & Karmiloff-Smith, 2002; Campbell et al.,
1990; Campbell et al., 1997). For example, Campbell and her colleagues have described two cases of patients with left and right hemispheric lesions who did not exhibit any susceptibility to the McGurk effect (Campbell et al., 1990). These patients, however, also suffered from aphasia, alexia, and prosopagnosia, which could also presumably have accounted for their inability to process and integrate auditory- and visual-speech signals. Similarly, a patient with bilateral lesions in V5/MT was found impaired in his ability to correlate visual lip-movements with the corresponding auditory-speech, which could, however, be due to akinetopsia (i.e., a motion processing deficit; Campbell et al., 1997). Williams syndrome patients have also been shown to exhibit a disrupted ability to integrate audiovisual speech, but this could probably be due to the visuospatial processing deficits in patients suffering from this syndrome (Böhning et al., 2002). Finally, neglect patients (i.e., inability to report, react, or search for stimuli located in the space contralateral to the patient’s lesion) have shown evidence of a temporal distortion, which, however, is often confounded with the spatial deficits of this condition (Baylis et al., 2002; Becchio & Bertone, 2006; Rorden et al., 1997).

The difficulty to isolate disruptions specific to multisensory temporal integration, in addition to the malleable perception of synchrony (i.e., flexible mechanisms, percept that changes depending on stimulus qualities and measurement tasks; e.g., Vatakis, 2013), make the topic particularly challenging to study in clinical populations. In the following pages, we will review evidence that show cases of specific impairment in the perception of synchrony in the absence of any other major deficiencies as well as cases where multisensory temporal integration is greatly impaired as a consequence of other dysfunctions. We will also review cases where the research is as yet limited but potential impairment in multisensory temporal integration may be critical in terms of treatment, diagnosis or both. The reader must note that we mainly focused on reviewing multimodality and not unimodality. Thus, unimodal stimulation/experimentation is covered only when necessary.

### 3 Multisensory Temporal Integration: Specific Disruptions or Consequence of Other Deficits?

#### 3.1 Case Reports

I told my daughter her living room TV was out of sync. Then I noticed the kitchen telly was also dubbed badly. Suddenly I noticed that her voice was out of sync too. It wasn’t the TV, it was me.

PH’S experience as reported in *New Scientist*, 2013
A specific disruption of the ability to integrate audiovisual speech has, in fact, never been reported until recently in two separate patient cases. First, in 2006, Hamilton, Shenton, and Coslett described a patient – AWF – who reported experiencing a temporal mismatch between the auditory- and visual-streams of a speech signal in the absence of any language or sensory impairment. AWF reported a difficulty in understanding face-to-face speech and described his experience as if “watching a movie with the audio out of sync” (Hamilton, Shenton, & Coslett, 2006). Imaging data from this patient revealed a biparietal hypoperfusion with prominence in the right region of the brain. In order to evaluate the deficit objectively, AWF was subjected to various behavioral tests, including a digit span task (with auditory-only or audiovisual presentations), a word-to-picture matching task (where auditory words were paired with congruent/incongruent facial movements, or no images), and a McGurk task. AWF exhibited a substantial impairment on a variety of these tasks, with the greatest impairments observed under conditions where multiple sensory inputs were presented, while no unimodal deficits were detected (through a visual/auditory temporal order judgment – TOJ – task using simple stimuli; i.e., judging the order of stimulus presentation). For instance, the patient’s performance was lower in the digit span task in the presence of a face as compared to the no face condition and slower (but accurate) in the word-to-picture matching task when simultaneous audiovisual speech stimuli were presented. Thus, AWF appeared unable to efficiently integrate the auditory- and visual-streams of related multisensory events. The authors, therefore, focused on the integration abilities of AWF suggesting that the parietal cortical injury was potentially responsible for his desynchronized experiences without, however, providing much data on those experiences.

AWF’s case (although insufficiently described) showed, for the first time, that the experience of desynchronized events is not improbable (Hamilton, Shenton, & Coslett, 2006), yet the direction (i.e., sensory stream leads/lags) and other details (e.g., width of TWI) of the experience were not reported, leaving us unable to paint a detailed picture and make specific hypothesis on the mechanisms governing audiovisual synchrony perception. While waiting for the next publication on AWF’s case, another unique patient – PH – made his appearance in 2013, in an article by Freeman and colleagues. Specifically, the authors described PH, who had asynchronous speech experiences with the auditory stream (i.e., voices) preceding the visual (i.e., lip/facial movements). The medical history of PH included a surgery for treatment of pericarditis, a subsequently developed generalized myasthenia gravis, and, finally, 2–3 months later a sudden onset of timing distortions. Currently, there is no evidence linking myasthenia with timing. High-resolution magnetic resonance
imaging (MRI) and diffusion tensor imaging (DTI) revealed that PH had lesions in pons and basal ganglia, both of which are areas associated with timing and multisensory processing. Behaviorally, PH was thoroughly tested so as to address whether or not the experienced asynchrony interrupted integration processes, thus, the authors examined the potential association or independence of the mechanisms governing event synchrony and unity (e.g., Spence & Squire, 2003; Vatakis & Spence, 2007).

PH along with a group of older and younger healthy controls (M = 65 and 22 years of age, respectively) was evaluated in a TOJ and identification task using both simple (stream-bounce illusion) and complex stimulus experimental set ups (e.g., McGurk effect; Freeman et al., 2013). PH’s data verified his reported experiences. That is, his performance resulted in a point of subjective simultaneity (PSS) of 210ms auditory speech lagging visual speech, thus requiring visual speech to be presented first by a large interval for synchrony to be perceived. In speech identification, the opposite pattern was observed, with PH requiring 240ms auditory lead for optimal McGurk fusion. Comparison of PH to the controls showed larger deviations for the patient in terms of PSS and speech identification but much smaller just noticeable differences (JND) values as compared to the other two groups. No differences were noted in terms of the perception of synchrony for non speech stimuli. One particularly intriguing finding was the similar behavioral pattern exhibited by both PH and some controls, where the auditory/visual lead/lags noted in the TOJ task (synchrony perception) were inverted for the identification task (integration). These findings led the authors to suggest that it may be the case that the perception of synchrony and of integration depend on distinct timing mechanisms. Furthermore, they suggested the idea that the discrepancies in timing between mechanisms are not minimized (as previous claimed; e.g., Spence & Squire, 2003), but rather perceived relative to the average timing of these mechanisms. This idea was formulated in a theory, the ‘temporal renormalization theory’, which is one of the first to propose some kind of averaging between mechanisms for the percept of synchrony.

In 2008, we also worked with a patient – RW – whose case resembled those of AWF and PH (Vatakis, 2008). In particular, RW reported perceiving auditory-speech as occurring earlier than the corresponding visual-speech. This desynchronized experience was heightened when he watched television and, particularly, when he watched people singing. RW reported experiencing this desynchronization for 3 years prior to testing, had no history of neurological disease or any cognitive difficulties, and was not taking any medication. Initially, RW was evaluated through a simultaneity (SJ) task (i.e., judging if a stimulus was synchronous or not) for audiovisual speech (a female uttering /da/) and
non speech (a complex harmonic tone paired with a white bar) stimuli. The results showed that RW indeed appeared to require a much larger auditory lead as compared to controls, while this was not the case for non speech stimuli. Given, however, that only a small number of stimuli were tested along with the fact that musical stimuli were not evaluated, RW was retested. Retesting included speech and musical stimuli in a TOJ task (see Vatakis & Spence, 2006; for design and stimuli). The reassessment showed no differences from healthy controls for both the musical and speech stimuli. Difficulty of access to RW did not allow further testing, the results, however, showed that RW did not have strong and consistent timing distortions (as he never reported problems in face-to-face communication) or it could also be the case that the experienced symptoms were no longer present at the time of testing.

Although such case studies are rare, they do show that impairments focused only in timing are probable. Thus, it could be the case that synchrony perception stems from a “renormalization” process (Freeman et al., 2013), however, further investigation is needed to explain: (a) why both RW and PH experienced auditory leads in their “out-of-synch” experiences? (b) why was speech the sole stimulus that was impaired? (c) could it be the case that predictive cue processing is also impaired in these patients, thus potentially affecting the renormalization process? (d) can synchrony and binding mechanisms truly be independent or rather in continuous “collaboration”?

3.2 Schizophrenia

Time has stopped; there is no time... The past and future have collapsed into the present, and I can't tell them apart.

The experience of an acute schizophrenic patient as reported in Melges, 1982, p. xix

Schizophrenia (SZ) is characterized by delusions, hallucinations, disorganized thinking, abnormal motor behavior (including catatonia), and/or negative symptoms (American Psychiatric Association, 2013). SZ has also been associated with a distorted sense of time continuity as reported by patients and clinicians (e.g., Gómez et al., 2014; Melges, 1982; Minkowski, 1933), as well as with behavioral and neuronal sensory processing abnormalities (e.g., Williams et al., 2010). The temporal and sensory implications in SZ have led to the investigation of potential impairments in multisensory integration (Tononi & Edelman, 2000), with the majority of research focusing on audiovisual (synchronous) speech (most often through the use of the McGurk effect; e.g., de Gelder et al., 2003; Pearl et al., 2009; Ross et al., 2007; White et al., 2014). A number of these studies have showed impaired speech integration, however,
deficits have also been identified for simple stimuli. For instance, tasks such as backward masking (e.g., Saccuzzo & Schubert, 1981) have shown that schizophrenics require longer temporal separation of the target and mask in order to effectively locate, detect, or identify the given target.

Findings implicating larger temporal separation between stimuli in sz (e.g., Saccuzzo & Schubert, 1981), led Foucher and colleagues (2007) to propose that integration per se may not be impaired but rather temporal processing. They examined this hypothesis by measuring simultaneity thresholds for unimodal (auditory, visual) and bimodal (audiovisual) stimuli in schizophrenics and healthy controls. Participants’ performance validated the proposed hypothesis with patient data revealing wider temporal windows in all conditions as compared to the controls (Visual: 37 ± 15 vs. 27.5 ± 8ms, Auditory: 42.7 ± 16 vs. 30.5 ± 17ms, Audiovisual: 265 ± 86 vs. 203 ± 51ms, for patients vs. controls, respectively; but see Schwartz, Mallott, & Winstead, 1988). Further analysis showed that performance in all three conditions was highly correlated, thus verifying that the observed effects were not driven by a specific sensory impairment but distorted timing instead. The authors suggested that there might be a link between the extended temporal windows observed in their study and previously reported time estimation impairments in sz. They further speculated that this association could be based on the disordered activation of the cerebellum (Andreasen, 1999; Minkowski, 1933) or the potential dysfunction of the basal ganglia (e.g., Lacruz et al., 1991), but as yet this has not been elucidated. It must be noted here that if synchrony and integration are two separate processes, this study shows differential temporal processing but does not address whether multisensory binding is intact or impaired in sz.

Giersch and colleagues (2009) re-examined temporal discrimination thresholds in sz by eliminating potential decisional (e.g., higher probability to assume synchrony in an sj task) and attentional biases (e.g., attentional effects due to stimulus onset cues and spatial presentation). They, therefore, presented two target stimuli in different locations with synchronous or asynchronous luminance changes (see Elliott et al., 2007). Data from stabilized chronic outpatients and matched controls replicated Foucher et al.'s (2007) findings, with the patients exhibiting longer simultaneity thresholds as compared to controls, thus further supporting the idea that sz is associated with a timing distortion.

The above-mentioned findings demonstrate the maintenance of event integration in sz (but see e.g., Ross et al., 2007) over longer twi. Clinical evidence, on the other hand, describe the experience of a fragmentation of events in time. This disparity was investigated by Lalanne, van Assche, and Giersch (2012a) using the Simon paradigm (Simon & Wolf, 1963). Specifically, they
presented, within the TWI, two stimuli in or out of synchrony on the same or different locations on the screen, while participants responded using the left- and right-sided keys for simultaneity and asynchrony, respectively. It was expected that for same-side presentations, the participants should be biased towards the side of the stimulus (classical Simon effect), while for opposite side presentations, a bias was expected only for the asynchronous cases (although not perceived by the participants). Specifically, for the latter, if the first stimulus was detected as an isolated event on a particular location then responding should be biased to that location, while if a second stimulus was anticipated a bias should be expected to the location of the second stimulation (see also Lalanne et al., 2012b). Performance from stabilized outpatients (on medication) and healthy controls replicated, for one more time, the higher detection thresholds in SZ (Schmidt et al., 2011). Most importantly, it was shown that for shorter SOAs, the patients showed a clear bias towards the location of the first stimulus, while for larger SOAs both participant groups were biased towards the location of the second stimulus (Lalanne et al., 2012b). These findings were interpreted according to the predictive coding theory, with patients processing stimuli in a feed-forward way, having impaired prediction for the second stimulus, thus treating each stimulation as isolated rather than part of an event sequence.

The existence of an extended TWI implies higher levels of integration, however the Lalanne, van Assche, and Giersch's (2012a) findings of sensitivity to short asynchronies imply less integration (Vatakis & Spence, 2007; Welch & Warren, 1980). Given these conflicting views, Martin and colleagues (2013) studied the potential differences of implicit and explicit temporal processing and, thus, focusing on the relationship of timing and integration in SZ. Using the McGurk paradigm with stimuli in or out of synchrony, the participants were required to complete both an identification and SJ task. The identification task allowed for measuring integration (implicit timing), while the SJ task served as an explicit measure of timing. Such task comparisons have resulted in null effects in healthy participants (e.g., van Wassenhove et al., 2007; but see Freeman et al., 2013). Patients and controls showed no differences in the rates of McGurk fusion or combination and unimodal (visual and auditory) speech recognition. Thus, showing intact audiovisual speech integration in SZ (see also Surguladze et al., 2001). Differences, however, were found in the width of the TWI, with patients requiring smaller auditory leads for fusion stimuli and larger auditory lags for combination stimuli compared to controls. Thus, showing speech integration to be less tolerant in patients than in controls. This finding was in direct contrast with the SJ results, where patients showed TWIs larger (yet not significantly) than those of controls. These findings support
previous reports of unimpaired integration and problematic timing, providing evidence for a potential dissociation of integration and synchrony timing mechanisms (as in Freeman et al., 2013).

The findings of distorted timing and intact integration capabilities are not limited to sjs but have also been observed in other temporal tasks. de Boer-Schellekens et al. (2013) utilized, for the first time, tojs in a temporal ventriloquism paradigm (i.e., the presence of a beep before or after a flash alters the temporal percept of the flash as appearing earlier or later, respectively; Morein-Zamir, Soto-Faraco, & Kingstone, 2003). Adults with sz (on medication; 7 on co-medication) and healthy controls completed a visual toj task, with white squares presented above or below the fixation with or without the presentation of auditory stimuli before or after the visual stimulation (0, 100, 200 or 300ms). Results showed worse jnds for patients as compared to controls (28.4 vs. 21.6ms, respectively) for the smaller soas tested, while the presence of auditory stimulation lead to equal performance improvement for both groups. In terms of the pss, the patient group demonstrated higher ‘up-first’ responses as compared to controls (10.1 vs. −5ms, respectively; negative values indicating ‘down-first’ presentations), while no effect of medication or symptom severity was found. The results of this study replicate those reporting an extended twi but successful event integration. Additionally, they partly support the dysconnectivity hypothesis (i.e., impaired integration could lengthen neural conduction times and, in turn, lead to delayed action potentials and sensory streams not arriving in synchrony; e.g., Foucher et al., 2007) for the jnd differences obtained at the lower soa range tested, but not the null effects for the higher end of the soa range.

Given the known toj and sj differences in measuring synchrony perception (e.g., García-Pérez & Alcalá-Quintana, 2012; Vatakis et al., 2008) and the differential findings for longer vs. shorter intervals (e.g., de Boer-Schellekens et al., 2014; Lalanne, van Assche, & Giersch 2012a; Martin et al., 2013), Capa and colleagues (2014) compared patient performance in tojs and sjs utilizing the same stimuli. This experimental set-up allowed them to address whether sz is associated with distorted temporal ordering, in which case tojs should be afflicted more than sjs, or with distortions only at brief time intervals, in which case both tasks should be afflicted at the same level. Data from stabilized patients (on medication) and healthy controls revealed major performance impairments in patients in the toj task, which was also maintained for larger soas. Additionally, the patients’ error rate in the toj task (14 vs. 5% in controls) was higher than that predicted from their sj performance (i.e., in larger asynchronies the patients could complete the sj task but had difficulty in deciding order for the toj task). These results, therefore, point to a generalized distortion of ordering in time rather than one limited to very brief intervals.
The consistent finding of an extended TWI for SZ is equivalent to an extended experience of simultaneity, which, in turn, can be interpreted as an extended integration of past and present events and, thus, an altered structure of conscious experience (Husserl, 1991). Schmidt and colleagues (2011) examined whether or not these distorted experiences are specific to SZ or rather general to psychosis. They, thus, tested chronic schizophrenic (on medication) and first-episode psychosis (FEP of various diagnoses; on medication) patients along with healthy controls on an SJ task (as in Elliott et al., 2007, using a staircase procedure). The results of this study replicated the existence of an extended TWI for schizophrenics but also demonstrated – for the first time – that FEP patients exhibit higher simultaneity thresholds as compared to controls. These findings (although with a small N) point out the potential of altered timing in psychosis in general, rather to a specific disorder, thus putting forward the need for comparisons of different clinical populations or of studies with different populations but similar experimental set-ups.

Overall, there is a consistency in the findings pertaining to SZ and multisensory temporal processing. That is, schizophrenics maintain their ability to integrate audiovisual (as no study to date have examined other modalities) events but this integration happens over an extended TWI. Given that simultaneity and order are necessary for the perception of an event and that of a series of events linked in time, the timing distortion in SZ may also be associated with the disorganized speech and action understanding/execution impairments reported in SZ (e.g., de Gelder et al., 2003; Delevoye-Turrell et al., 2007). All of the experimentation, however, has focused on simple stimuli, thus it would be interesting to see how multisensory speech or other stimuli are integrated. Additionally, it would be interesting to see how this extended TWI affects both time estimation and sequencing tasks for simple and complex actions in SZ.

3.3 Autism Spectrum Disorders

Sometimes the channels get confused... Sometimes I know that something is coming in somewhere, but I can't tell right away what sense it's coming through.

Cesaroni & Garber, 1991, p. 305

Autism spectrum disorder (ASD) is characterized by impaired social communication and interaction and restricted, repetitive patterns of behavior, interests, and/or activities (American Psychiatric Association, 2013). Temporal processing distortions have also been reported in ASD, however, the empirical literature is limited with the majority of research been initiated during the last
few years. This research activity has shown that children with ASD experience difficulties with mental time travel, time estimation, and time continuity (e.g., Allman, DeLeon, & Wearden, 2011; Szelag et al., 2004), potentially due to a hypothesized critical deficit in the temporal synchronization between local and distributed neural networks (Brock et al., 2002).

ASD has also been associated both through autobiographical and caretaker reports (e.g., Cesaroni & Garber, 1991; Iarocci & McDonald, 2005) with sensory abnormalities such as: hyper/hyposensitivity to sensory stimulation, sensory distortions (e.g., Rogers, Hepburn, & Wehner, 2003; Waterhouse, Fein, & Modahl, 1996), problematic processing of multiple sensory inputs simultaneously (e.g., Brandwein et al., 2013; Bryson, 1970, 1972; Collignon et al., 2013; Foxe et al., 2013; Lovaas & Schreibman, 1971; Lovaas et al., 1971; but see Haviland et al., 1996; Loveland et al., 1995; Walker-Andrews et al., 1994), and difficulties identifying the sensory origin of an input (e.g., Cesaroni & Garber, 1991; O’Neill & Jones, 1997). Yet, the actual validity or importance of sensory disturbances in ASD is often put in question (e.g., Ashwin et al., 2009; Bonnel et al., 2003; Magnee et al., 2008; Mongillo et al., 2008), as evidenced from the removal of this issue from the DSM versions following DSM III (American Psychiatric Association, 1980) and its reintroduction in the DSM-5 (American Psychiatric Association, 2013). The wavering noted in the DSM guidelines has also been noted in research where the potential impaired sensory and multisensory processing hypothesis has not always been verified, in addition to the limited generalization of past findings due to small population sizes, absence of comparison groups, variable or unreported symptom severity, task difficulty, and variable – in terms of age and diagnosis-population groups (e.g., Bedko et al., 2006; Foxe et al., 2013; Kolko, Anderson, & Campbell, 1980; Lovaas et al., 1971; Woynaroski et al., 2013).

A number of studies have looked at multisensory temporal processing in ASD utilizing simple, well-studied paradigms such as the sound induced flash illusion (SIFI; i.e., a brief flash paired with two auditory beeps is actually perceived as two distinct flashes; e.g., Shams, Kamitani, & Shimojo, 2000). First, van der Smagt, van Engel, and Kemner (2007) examined low-level audiovisual integration in high-functioning adults with ASD and healthy controls (IQ matched) through the SIFI. Participants were presented with a series of auditory (beeps) and visual stimuli in 3 visual conditions (1, 2 or 3 flashes) combined with 4 auditory conditions (0, 1, 2 or 3 beeps), and, thus, including consistent and inconsistent (i.e., different numbers of beeps/flashes) stimulus pairings. The performance of flash detection showed that the number of concurrently presented sounds influenced the perceived number of disks similarly for both participant groups. Thus, indicating intact integration of auditory and
visual information at an early level of processing in ASD (but see Collignon et al., 2013). Given, however, that SIFI is highly dependent on the presentation timing of the auditory stimuli, Foss-Feig and colleagues (2010) conducted the exact same study with the addition of a timing manipulation. They tested children with ASD and typically-developing (TD) children matched in verbal/nonverbal cognitive abilities, reading level, and gender. Analysis of the participant reports on the number of flashes perceived showed that the ASD group experienced the illusion over a wider range of SOAs as compared to the TD group, with the TWI in ASD being double the size of that observed in TD children (Kwakye et al., 2011). The results from these two studies, therefore, support that integration is possible in ASD for simple stimuli but temporal processing seems to be impaired.

Shifting to more complex and social stimuli, Bebko and colleagues (2006) focused on defining whether or not people with ASD have impaired multisensory temporal integration capabilities when confronted with speech or action-related stimuli. They utilized a preferential looking paradigm so as to avoid instructions and/or task demands influencing participants’ performance. They tested 3 groups of participants: children with ASD, children with other developmental disabilities, and TD children, using three different types of audiovisual stimuli: (a) non linguistic (segment of a children’s game with a ball moving through a series of plastic ramps and cliffs along with the respective sounds), (b) simple linguistic (a woman counting at approximately one number per 1.5 s), and (c) complex linguistic (a woman telling a story). The analysis for looking away behavior showed more looking away time for simple linguistic as compared to non linguistic stimuli but no group interaction was noted. In terms of response to the asynchrony presented, ASD children showed no difference from chance performance in preference of synchronous versus asynchronous displays. Additionally, although there was a preference for synchronous displays of non linguistic stimuli in ASD, no interaction of stimulus type with participant group was obtained, instead only a main effect of stimulus type was noted. Thus, although this study utilized a low in demands task and a balanced group of participants, the results did not provide a clear picture of the multisensory temporal processing capabilities in ASD.

Further investigations utilizing complex stimuli with a focus on speech extended on the work first conducted by Bebko et al. (2006), resulting in a still conflicting picture. For example, Grossman, Schneps, and Tager-Flusberg (2009) examined whether individuals with ASD can integrate visual- and auditory-speech information presented in a meaningful linguistic context at normal speaking rate. Adolescents with ASD and TD controls matched in age, verbal IQ, and receptive vocabulary were tested. Participants completed an SJ
task for a 3-s video of a woman describing the baking of various desserts with the audiovisual streams presented in: synchrony, high slip rates (10, 12 or 14 frames), or low slip rates (4, 6 or 8 frames; 4 frames ~ 120 ms). The results showed that ASD participants were as accurate as their TD peers at all slip rates, thus showing normal integration of speech stimuli in ASD. It must be noted, however, that the null results could have been driven by: (a) the potential adaptation to the asynchrony due to the long video duration, (b) the hypothesized developmental “catch-up” noted in ASD, and/or (c) the mild severity of the symptoms of the participants tested. Regarding the latter issue, Woynaroski and colleagues (2013) examined unisensory and multisensory processing capabilities in ASD along with symptom severity. ASD and TD participants were presented with McGurk stimuli in matched or mismatched formats and with the sensory streams either in synchrony or asynchronously. The analysis revealed intact auditory but impaired visual and audiovisual speech perception in ASD in comparison to the TD group. Deficits were also noted in the case of non-verbal responding with poor performance in visual-only and audiovisual matched stimulus presentations. Additionally, a wider T11 was observed for the case of mismatched stimulus presentations with visual speech influencing mismatched speech reports more in ASD than in TD. Finally, in terms of symptom severity, it was found that performance in matched speech was highly correlated with communication-related symptoms and fusion percepts were highly correlated with sensory processing symptoms. Overall, therefore, this study showed a wide range of deficits for visual and multisensory temporal processing in ASD, which was associated with some ASD symptoms.

In an attempt to further elucidate multisensory temporal integration in complex stimuli not limited to speech, de Boer-Schellekens, Eussen, and Vroomen (2013) conducted a study utilizing T0Js and a range of audiovisual stimuli from simple (flash-beep) to more complex ones with or without social aspects (i.e., hand clap and speech – a Dutch female uttering /bi/). High-functioning adolescents in the autism spectrum (patients with autism disorder, Asperger’s syndrome, and pervasive developmental disorder not otherwise specified, PDD-NOS) and TD controls (age-, gender-, and IQ-matched) completed the TOJ task revealing that the ASD group had larger JNDSs than the control group for all conditions tested. Thus, demonstrating that ASD individuals suffer from a generalized impairment in audiovisual temporal processing, which is not limited to speech. Overall, all groups performed best for the hand clapping condition and, subsequently, for the simple flash-beep and speech stimulation. Based on the fact that both groups performed best with the clapping hands, a condition that involves anticipatory visual information, suggests that individuals with ASD can use predictive information. Given that this study
had a very specific set of patients and limited population size, Stevenson et al. (2014) conducted a similar study with a large sample of ASD (Autism = 25%, Asperger = 66%, and PDD = 9%) and TD age-matched individuals. The participants were presented with audiovisual stimuli of simple flashes and beeps, dynamic handheld tools, and single syllable utterances (/ba/ and /ga/) and completed an SJ task for all conditions, a McGurk task for the speech stimuli, and unimodal (auditory and visual) TOJ tasks for the simple stimulus conditions. Participants' performance revealed a strong link between multisensory temporal processing and speech perception in ASD. Specifically, the poorer an individual’s temporal acuity across vision and audition (i.e., larger TWI), the weaker their ability to bind auditory and visual speech to create a robust McGurk percept and to integrate multisensory stimuli in general. The better an individual’s multisensory temporal acuity, the more reliable perceived synchrony was as a predictor of integration (i.e., whether or not two sensory signals originated from a single external event simultaneously and should, thus, be perceptually bound). The width of the TWI for both participant groups was found to be dependent on the complexity of the stimuli presented, with the largest widths obtained for speech (e.g., Vatakis & Spence, 2006). In ASD, there was a particularly enlarged window for speech as compared to the rest of the stimuli (Bebko et al., 2006). Finally, there was also a marginal effect of diagnosis (collapsed across stimulus types), suggesting impairments for the cases of simple stimulus presentations across the different groups in ASD (de Boer-Schellekens et al., 2013; Foss-Feig et al., 2010; Kwakye et al., 2011). Although this study tested participants from 6 to 18 years of age, no separate analysis by age group was conducted. The authors interpreted their speech findings as an effect driven by either long processing times for speech perception or extended processing times within each sensory stream of the speech signal, and, thus, interpret these as supporting the temporal binding hypothesis of autism (Brock et al., 2002; but see Chan & Naumer, 2014).

Overall, the research conducted to date shows that ASD is associated with an extended TWI, but it remains to be clarified whether this extended window is limited to speech or generalized to all types of stimuli. One way to account for this debate in the literature is to further experiment with stimuli of different modalities and modality combinations using implicit or explicit paradigms (e.g., Wada et al., 2014). Additionally, implementation of complex stimulation should take into consideration issues related to semantics and emotional content and, thus, experiment with stimulation that is controlled for social-related activities (e.g., Bakirtzi & Vatakis, 2014). Further experimentation should also consider in detail sample size and population selection both for the ASD and the TD group. For instance, participants in the ASD group should also be
screened for undiagnosed attentional deficits, while the TD group should be screened for ASD-related symptoms. On the latter topic, Donohue, Darling, and Mitroff (2012) conducted a study on multisensory processing and ASD-related symptomology in an adult, *non-clinical* population. Specifically, they tested 101 participants on the Autism Spectrum Quotient (ASQ) questionnaire (commonly used as a screening measure; covers issues under the categories of social skill, attention switching, attention to detail, communication, and imagination) and a multisensory SJ task. Analyses revealed that the PSS correlated significantly with the scores on the ASQ, with higher ASQ scores (i.e., higher ASD symptomatology) being associated with an auditory-first bias in responding (Russo et al., 2012). This association could be related to higher auditory processing sensitivity and/or auditory effects on attention and, subsequently, to a potentially larger TWI that is auditory shifted.

3.4 *Attention Deficit Hyperactivity Disorder*

Attention deficit hyperactivity disorder (ADHD) is prevalent in children and it is characterized by a persistent pattern of inattention (i.e., being disorganized, wandering off, difficulty in sustaining focus independent of disobedience or lack of understanding) and/or hyperactivity (i.e., excessive motor activity) and impulsivity (i.e., actions without forethought, potentially harming, that result in immediate rewards) that interferes with functioning and/or development (American Psychiatric Association, 2013). Timing distortions have also been noted in ADHD but mainly in terms of time estimation (e.g., Seri et al., 2002; Smith et al., 2002; Wittmann et al., 2011) with the majority of the findings showing impulsivity to result to poor motor inhibition and, thus, interval underestimation (Brown & Vickers, 2004; Smith et al., 2002). Such distortions have been associated with basal ganglia dysfunction (Meck, 1996), but alternative or complementary accounts put forward a potential working memory deficit (Brown & Vickers, 2004). More recently, the association of hyper-responsive superior colliculus (SC) with increased distractibility makes for an alternative model for ADHD pathology (Overton, 2008).

Potential distortions in temporal processing in ADHD have rarely been investigated. The only investigation on the topic is the study by Brown and Vickers (2004) using simple visual stimulation in adolescent ADHD patients. Specifically, they investigated the perceptual nature of the temporal deficits previously reported in ADHD by minimizing memory and motor-related demands, as well as task complexity. ADHD patients (tested on- and two days off-medication) and healthy controls (age- and gender-matched) completed a verbal SJ task (in a staircase paradigm) for pairs of red light emitting diodes (LEDs). The LEDs were presented bilaterally and unilaterally over a set of different SOAs.
Participants’ performance revealed no temporal processing differences in ADHD participants (on- or off-medication) as compared to controls (mean thresholds: 30 and 31ms, respectively). Given these null results as compared to the time estimation studies, the authors argued against the basal ganglia dysfunction account for ADHD. It must be noted however that the small sample tested, the absence of younger population (as it is usually the case for ADHD), and the unimodal nature of the study render these results preliminary.

Given the limited amount of research on the topic, the involvement of attention in multisensory temporal integration (Talsma et al., 2010), and the recent proposal of SC involvement in ADHD (an area known for its involvement in multisensory integration; Stein & Stanford, 2008), it is pertinent to investigate more thoroughly whether or not ADHD patients do exhibit multisensory temporal integration deficits (Panagiotidi, Stafford, & Overton, 2014) and how these potential deficits associate with those reported in time estimation.

3.5 Aphasia

A word is a sequence of auditory events (phonemes)... suppose that an individual loses the capacity for identifying the correct order of phonemes. The word ‘electrician’ ‘i lek’ tris’ an’ might as easily be interpreted as ‘tris’ lek’ an’ or as’an i tris’ lek’.

Efron, 1963a, p. 404

Aphasia is associated with the loss of one’s ability to speak and/or comprehend language along with the inability to read and write, usually caused by stroke or brain tumor. Research on aphasia has focused on the identification of the disrupted cognitive processes underlying language, along with the classification of aphasia depending on the symptoms and the brain areas affected (e.g., Charidimou et al., 2014). Efron (1963a), however, proposed that aphasia may be related to impaired temporal processing emphasizing the importance of correct phoneme ordering in language and the aphasic symptoms of jargon, neologisms, and "word-salad" in speech. In addition, data from Efron and others (e.g., Efron, 1963b,c,d; Nicholls, 1996) support that simultaneity and temporal order are processed in the hemisphere dominant for speech (Wittmann et al., 2004).

Based on this hypothesis, Efron, in his 1963a study, examined patients with lesions of the left hemisphere (LH; with some degree of aphasia) or the right hemisphere (RH) in the same general areas, and patients with no aphasia (matched in age and general alertness). The patients were asked to complete a
visual and an auditory tertiary task (i.e., reporting synchronous or asynchronous presentations and in the case of asynchrony reporting of order; the “I do not know” option was also available) using simple stimulation. Analysis revealed order distortions for the patients with LH lesions (and some degree of aphasia) only, thus supporting the association of hemispheric dominance and aphasia (but see Sherwin & Efron, 1980) with timing. Results also showed that ‘expressive’ aphasics (i.e., clear understanding of speech but no standard intonation, speech is slow and staggered with long breaks) had worse auditory discrimination performance as compared to visual, while “receptive” aphasics (i.e., inability to understand normal speech, generation of speech with the right intonation and speed is possible, but words are not meaningfully combined) showed the reverse pattern. Although one of the first studies to explore the link of timing and aphasia, the sample size tested was quite small, thus making the generalization of the results and the mainstreaming of the idea difficult. Subsequent investigations, however, replicated Efron’s findings in terms of poor auditory discrimination thresholds in aphasia (e.g., Edwards & Auger, 1965; Holmes, 1965), but no such replications were reported for vision (Holmes, 1965; Jerger et al., 1969).

Given the methodological differences of the previously conducted studies (e.g., spatial location, different stimulus types, no stimulus control for intensity), Swisher and Hirsh (1972) conducted a study to clarify whether the previously noted temporal distortions in aphasia were valid or rather a methodological artifact. They, therefore, presented all possible stimulus configurations (i.e., visual/auditory: different color/pitch in the same or different location/ear with a color/pitch response, same color/click in different location/ear with a location response) to different patient (LH damage with receptive aphasia, LH damage with expressive aphasia and hemiplegia, RH hemiplegia with no aphasia) and healthy control (young and older participant groups) groups. Their results were similar to those obtained by Efron (1963a), with the presentation of different visual stimuli in the same location resulting to larger discrimination thresholds for the LH impaired as compared to the RH impaired patients. No such differences were noted for visual presentations in different locations. For auditory presentations, the deficits were greater in comparison to those for the visual modality with the receptive aphasics showing larger discrimination thresholds (see also von Steinbüchel et al., 1999) for presentations in the same as compared to different ears. Stimulation of different type and location improved performance for the LH patient groups. The greater effect observed in receptive aphasics for audition could be driven by a number of factors such as symptom severity as well as specific brain regions afflicted, yet it still supports Efron’s proposal of a close association of language function
and temporal processing (see also von Steinbüchel & Wittmann, 1997; Wittmann et al., 2004). This close association is as yet undefined given that limited research conducted in recent years and the absence of experimentation with multisensory stimuli.

3.6 **Dyslexia and Specific Language Impairments**

Developmental dyslexia has been repeatedly associated with impaired or slowed temporal processing (e.g., Farmer & Klein, 1995), a direct, however, association has not been accepted as yet (e.g., Protopapas, 2014). Unimodal visual and auditory impairments have lead to the hypotheses of impaired functioning of a specific modality, a general perceptual impairment or a speech-specific dysfunction that is associated with phonological processing (e.g., Laasonen et al., 2000). The use of unimodal as well as multimodal stimulation of nonlinguistic stimuli can provide insight as to the potential impairments in multisensory temporal processing, which is critical in the development of reading and language acquisition (e.g., Bremner, Lewkowicz, & Spence, 2012).

One of the first studies to examine the potential association of dyslexia and temporal processing both unimodally (i.e., clicks in the auditory, flashes in the visual, and indentations of the skin in the tactile modality) and multimodally was conducted by Laasonen and colleagues (2000). Specifically, they tested developmentally dyslexic readers and control readers through a within- and between-modality sJ task (using stimulus pulses in two trains for a constant interval on distinct spatial locations) along with a series of other tests. The data, overall, showed that the dyslexic group segregated spatiotemporal perceptual information at a slower rate than the control group. These differences were noted not only for unimodal presentations but also and more pronounced for bimodal ones with the highest differences noted for the audiovisual combinations presented. A subsequent replication (Laasonen, Service, & Virsu, 2002; Laasonen et al., 2001) utilizing adult participants and an additional TOJ task measure continued to show impairments but at a different level for each modality. Both tasks showed poor discrimination thresholds for the dyslexic group for all modalities and their combinations, but with auditory, tactile, and audiotactile stimulation measuring at the lowest performance as compared to the control group. Dyslexia, therefore, was associated with a generalized temporal impairment in perceiving rapidly presented sequential non speech events, which was found to deteriorate even more with age (Virsu, Lahtinnuuttila, & Laasonen, 2003).

The above-mentioned studies provide the first evidence of a multimodal temporal processing impairment in dyslexia. It is as yet unknown, however, whether or not multisensory temporal integration is also affected, given that a
potentially extended TWI could interfere with processes that require rapid and accurate integration of sensory inputs (e.g., reading; King, Wood, & Faulkner, 2007). A first investigation on this issue was undertaken by Hairston and colleagues (2005) using simple stimuli in a temporal ventriloquism paradigm (e.g., Morein-Zamir et al., 2003). Specifically, they tested dyslexic and typical-reading participants (IQ above 70) in a visual TOJ task (staircase procedure) and, subsequently, a visual TOJ task in the presence of synchronous or asynchronous auditory stimuli. The results showed impaired visual TOJs in dyslexia, as per previously mentioned studies. In terms of integration, in the presence of synchronous auditory stimulation, the dyslexic group performed significantly better compared to the unimodal performance, while no such difference was obtained for the control group. When auditory delays were introduced, the control group showed benefits for delays over 100ms and up to 250ms, while the dyslexic group benefited for delays as low as 50ms and as high as 350ms. Thus, exhibiting an extended TWI as compared to the control group. Similar results were obtained for audiovisual speech stimuli for children with specific language impairment (SLI; Pons et al., 2012), where auditory speech delays of up to 666ms went unnoticed when compared to a control group. These latter results could be attributed to dysfunctional predictive mechanisms of the sensory inputs for the percept of unified multisensory speech and/or extended TWIs.

The above-mentioned deviations of temporal processing and multisensory integration in dyslexia and SLI could be driven by an attentional impairment (e.g., spatial allocation of attention), which has also been under-researched (e.g., Hood & Conlon, 2004; Landerl & Willburger, 2010; Pons et al., 2012; Talcott et al., 2002). Further research is, thus, needed in the potential associations of timing, modality, and attention (Harrar et al., 2014) in dyslexia and SLI utilizing both simple and complex stimuli (Kronschnabel et al., 2014, for use of complex stimulation in terms of congruency but not timing).

3.7 Parkinson’s Disease
Parkinson’s disease (PD) is a neurodegenerative disease characterized by motor-related impairments (e.g., bradykinesia, rigidity, postural instability), as well as cognitive deficits, including timing distortions, which may be associated with executive dysfunction affecting approximately 30% of PD patients (Parker et al., 2013). The timing distortions noted in PD relate to time estimation, while data on temporal discrimination is sparse. Additionally, past studies have shown a large percentage of PD patients to exhibit primary sensory impairments (e.g., Koller, 1984; Snider et al., 1976). It is, however, unclear why these sensory and timing deficits occur. Some researchers promote basal
ganglia as a key contributor in these PD disturbances given its primary role in motor control and its involvement in sensory (Graziano & Gross, 1993; Snider et al., 1976) and sensorimotor integrative function (Artieda et al., 1992), but as yet no concrete conclusions have been reached.

A first set of investigations focusing on temporal discrimination using tactile (Lacruz et al., 1991) or proprioceptive (Fiorio et al., 2007) stimuli showed PD impairments, with discrimination thresholds being larger for the patients as compared to controls. As revealed by these studies, the stimulation location is critical since larger thresholds were noted for stimulation at the hand contralateral to the lesion or the affected arm in the case of unilateral bradykinetic rigid PD patients (Fiorio et al., 2007; Lacruz et al., 1991). A direct comparison of different modalities was conducted by Artieda et al. (1992) by measuring temporal discrimination thresholds for somesthetic, auditory, and visual stimuli in PD (grouped by severity: mild, moderate, severe) and healthy controls. Utilizing the method of limits, the authors asked participants to detect the number of sensory inputs (1 vs. 2) they were receiving. Analysis of these reports showed that PD patients were deficient in all three modalities and the degree of the deficit increased with symptom severity. This deficit was expressed with significantly extended TWI as compared to controls. Thus, in addition to other timing deficits noted in PD (e.g., time estimation, sensorimotor synchronization), the authors proposed that these effects may be due to slow running internal clocks, which, in turn, impaired patients’ temporal resolution for simple stimuli.

Results, although limited, support impaired temporal discrimination thresholds in PD when the stimulus input is presented unimodally. It is as yet unknown how PD patients perform in the presence of multisensory and complex stimulation. Given the data supporting the involvement of basal ganglia in multisensory input and timing (e.g., Graziano & Gross, 1993), it may be the case that the indirect basal ganglia circuit inhibiting neurons from thalamus to cortex is impaired given research suggesting dissociation of motor and temporal discrimination and direct basal ganglia circuits for movement (Lucas et al., 2013; Widnell, 2005).

Similar to PD, Dystonia is a neurological condition associated with impaired functioning of the basal ganglia and characterized by motor disturbances (repetitive movements, abnormal postures) in many different (generalized dystonia) or specific body parts (focal dystonia; e.g., focal hand dystonia, cervical dystonia) along with abnormal somatosensory processing (e.g., Tinazzi et al., 2004). A small number of psychophysical studies have shown that dystonic patients demonstrate distorted temporal discrimination with tactile and even visual stimuli (e.g., Aglioti et al., 2003; Fiorio et al., 2003). In terms of
multisensory temporal integration, recent studies have demonstrated deficits in visuo-tactile integration in generalized and focal hand dystonia, while visual temporal discrimination was found to be impaired only for generalized dystonia. Similarly, Tinazzi and colleagues found patients with cervical dystonia to exhibit poor tactile and visuo-tactile discrimination as compared to healthy controls, yet visual thresholds were normal. These differences may imply that each type of dystonia is governed by slightly different impairments localized at different neural circuits composing the basal ganglia. Thus, further understanding of basal ganglia dysfunction and the commonalities and differences of the various types of dystonia will allow us to also understand PD impairments.

4 Looking Forward to Further Experimentation

The perception of order and simultaneity are fundamental in the perception of unified multisensory events. We suggest that distortion at any level of the timing experience (simultaneity, order, duration) leads to a disruption to all other levels of our experience and collectively this disruption may be associated with an altered clinical picture. Current investigations, however, focus only on one of those levels of the timing experience, thus potentially ignoring associations/interactions that may be important for understanding a specific clinical case, a collection of symptoms, and/or the implementation of a particular intervention. Time estimation has been investigated more vigorously than multisensory temporal processing in the clinical domain. The few and recent studies focusing on the latter have shown, for the first time, a potential distortion of timing in the absence of any other impairments (see Section 3.1 of this chapter), timing being the critical component of a disorder (see Section 3.2 of this chapter), synchrony and binding being potentially differentiated in terms of timing mechanisms (see Sections 3.1 and 3.2 of this chapter), as well as timing distortions being co-present with other impairments, with the latter potentially causing the timing distortions noted (see Section 3.7 of this chapter).

In this chapter, we explored a range of different clinical/neurological cases that experimentation lead to findings of impaired sensory discrimination and mostly extended TWI (with some tendency for the auditory stream to be leading), while in a few studies we also obtained data regarding multisensory binding although concrete conclusions were not reached (see Table 1.1). The literature covered here may tempt one to claim that there is a single, common mechanism that governs all these distortions in timing and integration. This however will be premature, simplistic, and potentially wrong (e.g., Freeman et al., 2013; Martin et al., 2013, showing evidence of different timing mechanisms). For instance, the
TABLE 1.1  *A brief overview of all the studies reviewed in this chapter covering issues related to multisensory temporal processing.*

<table>
<thead>
<tr>
<th>Behavioral task</th>
<th>Stimulus type</th>
<th>Modality</th>
<th>Distortions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Abstract</td>
<td>Speech</td>
<td>Action</td>
</tr>
<tr>
<td><strong>Case study</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hamilton et al. (2006)</td>
<td>Match detection, Digit span, and others</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Freeman et al. (2013)</td>
<td>TOJ, Identification</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Vatakis (2008)</td>
<td>TOJ</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>ADHD</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Aphasia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Efron (1963a)</td>
<td>Ternary</td>
<td>✓</td>
<td>A, V</td>
</tr>
<tr>
<td>Swisher &amp; Hirsh (1972)</td>
<td>TOJ</td>
<td>✓</td>
<td>A, V</td>
</tr>
<tr>
<td>Author(s)</td>
<td>Task</td>
<td>Modality</td>
<td>Results</td>
</tr>
<tr>
<td>-----------</td>
<td>------</td>
<td>----------</td>
<td>---------</td>
</tr>
<tr>
<td>von Steinbüchel et al. (1999)</td>
<td>Ternary</td>
<td>A</td>
<td>Distortion multisensory experiences</td>
</tr>
<tr>
<td>Artieda et al. (1992)</td>
<td>sj modified</td>
<td>A, V, P</td>
<td>Poor discrimination thresholds for all modalities tested</td>
</tr>
<tr>
<td>Artieda et al. (1992)</td>
<td>Motion detection</td>
<td>P</td>
<td>Poor discrimination thresholds</td>
</tr>
<tr>
<td>Fiorio et al. (2007)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>parkinson's disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foucher et al. (2007)</td>
<td>sj</td>
<td>A, V, AV</td>
<td>Extended TWI</td>
</tr>
<tr>
<td>Giersch et al. (2009)</td>
<td>Change detection</td>
<td>V</td>
<td>Extended TWI</td>
</tr>
<tr>
<td>Schmidt et al. (2011)</td>
<td>Change detection</td>
<td>V</td>
<td>Extended TWI</td>
</tr>
<tr>
<td>Lalanne et al. (2012b)</td>
<td>Simon effect</td>
<td>V</td>
<td>Extended TWI; Short SOAS: First stimulus presentation bias</td>
</tr>
<tr>
<td>Martin et al. (2013)</td>
<td>sj, Identification</td>
<td>A, V, AV</td>
<td>Identification: Window width with smaller A leads for fusion and larger A lags for combination stimuli;SJ: Extended TWI; Normal binding</td>
</tr>
<tr>
<td>de Boer-Schellekens et al. (2014)</td>
<td>TOJ</td>
<td>V, AV</td>
<td>Poor discrimination; PSS differences; Normal AV integration</td>
</tr>
<tr>
<td>Capa et al. (2014)</td>
<td>TOJ, sj</td>
<td>V</td>
<td>Poor order discrimination for short SOAS</td>
</tr>
<tr>
<td>Behavioral task</td>
<td>Stimulus type</td>
<td>Modality</td>
<td>Distortions</td>
</tr>
<tr>
<td>-----------------</td>
<td>--------------</td>
<td>----------</td>
<td>-------------</td>
</tr>
<tr>
<td></td>
<td>Abstract</td>
<td>Speech</td>
<td>Action</td>
</tr>
<tr>
<td><strong>Dystonia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tinazzi et al.</td>
<td>SJ</td>
<td>✓</td>
<td>V, T, VT</td>
</tr>
<tr>
<td>(2004)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Autism</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bebko et al.</td>
<td>Preferential</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>(2006)</td>
<td>looking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>van der Smagt,</td>
<td>V detection</td>
<td>✓</td>
<td>V, AV</td>
</tr>
<tr>
<td>van Engel, and</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kemner (2007)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grossman,</td>
<td>SJ</td>
<td>✓</td>
<td>AV</td>
</tr>
<tr>
<td>Schneps, &amp;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tager-Flusberg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(2009)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foss-Feig et al.</td>
<td>V detection</td>
<td>✓</td>
<td>VA-V</td>
</tr>
<tr>
<td>(2010)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kwakye et al.</td>
<td>TOJ</td>
<td>A, V, AV</td>
<td>V: Normal, A: Poor discrimination, Extended TWI; Persistence of binding</td>
</tr>
<tr>
<td>(2011)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>de Boer, Eussen,</td>
<td>TOJ</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>&amp; Vroomen (2013)</td>
<td></td>
<td>V</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Authors</td>
<td>Task</td>
<td>Ability</td>
<td>Modality</td>
</tr>
<tr>
<td>------------------</td>
<td>--------------------</td>
<td>---------</td>
<td>----------</td>
</tr>
<tr>
<td>Woynaroski et al. (2013)</td>
<td>Recognition</td>
<td>✓</td>
<td>A, V, AV</td>
</tr>
<tr>
<td>Stevenson et al. (2014)</td>
<td>SJ, TOJ, Identification</td>
<td>✓ ✓ ✓</td>
<td>A, V, AV</td>
</tr>
<tr>
<td><strong>Dyslexia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hairston et al. (2005)</td>
<td>TOJ</td>
<td>✓</td>
<td>V, AV</td>
</tr>
<tr>
<td>Laasonen et al. (2000)</td>
<td>RIS</td>
<td>✓</td>
<td>A, V, T</td>
</tr>
<tr>
<td>Laasonen et al. (2001)</td>
<td>RIS, TOJ</td>
<td>✓</td>
<td>A, V, T</td>
</tr>
<tr>
<td><strong>Specific Language Impairment</strong></td>
<td>Preferential looking</td>
<td>✓</td>
<td>AV</td>
</tr>
</tbody>
</table>

Proprioreception (P); Auditory (A); Visual (V); Tactile (T); Temporal order judgment (TOJ); Simultaneity judgment (SJ); Stimulus onset asynchrony (SOA); Temporal window of integration (TWI); Rate of information segregation (RIS)
enlarged windows noted in dyslexia, schizophrenia, and ASD cannot be governed by the same mechanisms. That is, dyslexics have been shown to exhibit impairments in auditory and visual temporal processing (e.g., Hairston et al., 2005; Laasonen et al., 2001), while investigations with ASD have resulted in unclear findings with some studies showing auditory impairments only (e.g., Kwakye et al., 2011). These findings may be related to different types or levels of disruption in multisensory temporal processing. Thus, for instance, ASD has been associated with local hyperconnectivity and long-range hypoconnectivity, but dyslexia with proximal hypoconnectivity but distal hyperconnectivity (e.g., Williams & Casanova, 2010), while both disorders have been associated with cerebellum impairments (e.g., Hodge et al., 2010). On the other hand (see Section 3.2 of this chapter), patients suffering from SZ do exhibit an extended TWI but recent behavioral evidence support the idea of patients getting “stuck” on the first stimulus presentation and, thus, leading to impaired discrimination performance.

The recent hypothesis that multisensory temporal processing may be governed by separate mechanisms for synchrony and integration (e.g., Freeman et al., 2013) is also supported by recent imaging studies. Specifically, Stevenson et al. (2010, 2011) in an fMRI study utilizing audiovisual speech in or out of synchrony identified two subregions of the multisensory superior temporal cortex (STC), one responding to synchrony independent of integration and another responding to integration regardless of the timing of the sensory streams. A limitation was also noted with increased synchrony leading to higher probability of integration. Thus, although separate, the mechanisms do ‘collaborate’ for the achievement of a unified moment and, thus, ‘meaningful’ interval. Given the distortions of temporal integration of multisensory events in many of the disorders reviewed in this chapter (see also Chapters 3 and 5 of this book) it may be important to further examine STC in terms of integration (e.g., Pekkola et al., 2006), timing, and anatomical abnormalities (e.g., Boddaert et al., 2004). Parietal regions should also be studied further given that in SZ functional differences are also noted in regions that project directly to STC such as parietal regions in the dorsal visual stream (Doniger et al., 2002). These latter regions were also implicated in the case of the patient AWF (Hamilton et al., 2006). Thus, it may be the case that STC is core in the unified percept of synchronous or near-synchronous moments (Stevenson et al., 2011).

Overall, it is pertinent to better understand the role of timing in the clinical/neurological patient. Such understanding will allow for the study of timing and binding mechanisms, but most importantly will allow for the development of diagnostic and/or rehabilitation tools. In terms of the latter, given that a number of disorders have been associated with an enlarged TWI, Powers, Hillock, and Wallace (2009) showed that perceptual training can change
perceived SJs with the change depicting a true perceptual change rather that a short-lived training effect (as shown by a 1 week after-training post-test; see also Powers et al., 2012; see also Schlesinger et al., 2014, for narrowing of the TWI with feedback training). Given that we support an association of the different levels of the timing experience, changes of the width of the TWI will also lead to temporal discrimination and potentially time estimation changes. Further research looking at the different levels of the timing in the same paradigm, with identical multisensory stimulation, and the same group of individuals (healthy or not) will allow for a unified model of our everyday unified and continuously flowing in time experience.

Acknowledgments

This work has been supported by the European project COST ISCH Action TD0904 (<www.timely-cost.eu>) “Time In MEntaL activitY: theoretical, behavioral, bioimaging and clinical perspectives (TIMELY)” and co-financed by the European Union (European Social Fund, ESF) and Greek national funds through the Operational Program “Education and Lifelong Learning” of the National Strategic Reference Framework (NSRF) – Research Funding Program: THALIS-UOA-375737.

References


