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An auditory-neuroscience perspective on the development of selective mutism

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ABSTRACT

Selective mutism (SM) is a relatively rare psychiatric disorder of childhood characterized by consistent inability to speak in specific social situations despite the ability to speak normally in others. SM typically involves severe impairments in social and academic functioning. Common complications include school failure, social difficulties in the peer group, and aggravated intra-familial relationships. Although SM has been described in the medical and psychological literatures for many years, the potential underlying neural basis of the disorder has only recently been explored. Here we explore the potential role of specific auditory neural mechanisms in the psychopathology of SM and discuss possible implications for treatment.

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Selective mutism (SM) is characterized by consistent failure to speak/vocalize in specific social situations (e.g., at school) despite the ability to speak normally in other situations (American Psychiatric Association, 2013). SM typically involves impairments in social and academic functioning. Reported complications include school failure, social difficulties in the peer group, and aggravated intra-familial relationships (e.g., Bergman et al., 2002; Cunningham et al., 2004; Steinhausen and Juzi, 1996).

In the early 90s Black and Uhde (1992, 1995) reported an overwhelming incidence of avoidant disorder or social phobia in children with SM. These authors argued that SM should thus be treated as an extreme manifestation of

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social phobia. Although this position has been challenged by data indicating that parents, teachers, and clinicians do not necessarily report greater social anxiety in children with SM compared with children with social anxiety (Manassis et al., 2003), and that children with SM do not report greater social anxiety than children with social phobia alone (Yeganeh et al., 2003), the high comorbidity between SM and social anxiety has still shaped clinical practice to a great extent (Viana et al., 2009).

Notably, although many children with SM display shy temperament and social anxiety, only a very small portion of socially anxious children meet DSM diagnostic criteria for SM. This suggests that SM may involve a unique component that is absent in typical manifestations of social anxiety disorder. Thus, other factors, perhaps more directly associated with the core symptom of SM and their potential effect on speaking behavior should be considered. In the current opinion-report we describe evidence for the involvement of sub-optimal function of the auditory efferent system in the psychopathology of SM. First, we briefly describe findings delineating associations between auditory efferent activity and vocalization. We then describe a series of studies from our laboratory providing evidence for efferent aberrations in SM. Finally, based on the auditory aberrations discovered we discuss potential implications for the development of alternative treatments for children with SM. Importantly, the current report is not intended to provide a comprehensive review of the SM literature but rather to provide a neuroscience perspective on one of its potential neural generators.

1. The role of auditory efferent activity in vocalization

Because a specific inability to produce speech in certain circumstances is the hallmark of SM, it makes sense to consider possible anomalies in the neural mechanism supporting this specific behavior. Self-monitoring of one's own voice has a vital role in the development and enduring maintenance of vocalizations in both humans and animals (Oller and Eilers, 1988; Doupe and Kuhl, 1999). Continuous transaction between speech and hearing mechanisms (Curio et al., 2000; Borg et al., 2009; Ventura et al., 2009) enables constant monitoring of the quality of voice and speech, perception of external sounds while vocalizing, and prevention of desensitization due to possible overstimulation by self-vocalization (Hoy, 2002). Aberrations in auditory feedback induced via experimental manipulations such as the presentation of background noise (e.g., Lombard effect) or delayed auditory feedback result in significant alterations in vocalization in humans (e.g. Lee, 1950; Lamprecht, 1988) and animals (Osmanski and Dooling, 2009).

In humans, two distinct efferent mechanisms are known to be involved in monitoring and regulating vocalization: the middle-ear acoustic reflex (MEAR) and the medial olivocochlear bundle (MOCB) reflex. The neural circuit of the MEAR controls the contraction of the stapedius and tensor-tympani middle-ear muscles upon presentation of loud low-frequency sounds. This results in stiffening of the ossicular chain and subsequent attenuation of sound (Borg and Counter, 1989). When the MEAR is activated by self-vocalization, it is assumed to produce an anti-masking effect by attenuating potential overloading of the cochlea and thereby maintaining a fairly constant level of sensitivity that prevents interference by the speaker's own voice (Curio et al., 2000). Furthermore, activation of the middle-ear muscles during vocalization has been allocated an important role in reducing distortion, nonlinearities, and upward spread of masking (Borg and Zakrisson, 1975).

The sound-evoked MOCB reflex originates in the medial portion of the superior olivary complex on both sides of the brainstem and is activated via myelinated fibers that project directly onto the outer hair cells in the cochlea (Guinan, 2006). The functioning of the MOCB can be tested non-invasively in humans by means of contralateral suppression of otoacoustic emissions (Collet et al., 1990). Contralateral acoustic stimulation can attenuate, through fibers of the MOCB, the acoustic energy generated by outer hair cells activity and can be measured in the ear-canal (Guinan, 2010). The functional significance of the MOCB reflex is still debated. Most of the research regarding MOCB function during vocalization has been conducted in animals. Data from the singing cricket (Poulet and Hedwig, 2002) and mustached bat (Goldberg and Henson, 1998) suggest that during self-vocalization inhibitory activation of the MOCB takes place. In the singing cricket, for example, intercellular recordings indicated that presynaptic inhibition of auditory afferents and postsynaptic inhibition of an interneuron occur in phase with the song pattern. The authors postulate that inhibitory action decreases the auditory interneuron's response to self-generated sounds, and thus reduces self-induced desensitization (Poulet and Hedwig, 2002).

In humans, the functional role of the MOCB during vocalization is not fully understood (Robertson, 2009). Recent evidence suggest that MOCB feedback protects the ear from noise-induced cochlear damage caused by exposure to moderate sound intensities similar to those created by vocalizations in various natural environments (Maison et al., 2013). These authors propose that chronic self-stimulation by vocalization may present a significant damage risk to the ear without protection from efferent feedback, a hypothesis supported by the notion that the MOCB reflex is activated in anticipation of vocalization (Suga and Jen, 1975; Xie and Henson, 1998). The MOCB reflex has also been shown to play an anti-masking role in normal hearing subjects during signal detection/perception in background noise. For example, activation of the MOCB reflex improved threshold detection and intensity discrimination of tones in noise (Micheyl and Collet, 1996; Micheyl et al., 1997), and enhanced perception of speech in background noise (Messing et al., 2009; Brown et al., 2010; Kumar and Vanaja, 2004; Giraud et al., 1997). Altered pre-neural amplification via outer hair cell activity that leads to an increase in signal-to-noise ratio for certain frequency bands has been suggested as a potential underlying mechanism for such improvements (Cooper and Guinan, 2006).

Valuable information regarding the functional role of MEAR and MOCB during vocalization may be gained by studying clinical populations that exhibit aberrations in

auditory efferent function. Altered MEAR has been reported in children with Williams syndrome (Gothelf et al., 2006), a rare genetic neurodevelopmental disorder affecting the cardiovascular system, central nervous system, connective tissue, as well as various brain regions. One of the more pronounced characteristics of Williams syndrome is hyperacusis (Gothelf et al., 2006; Blomberg et al., 2006). Gothelf et al. (2006) suggested that abnormal MEAR function may underlie hypersensitivity to sound leading these children to avoid noisy environments. Moreover, a recent study indicated that the severity of hyperacusis in Williams syndrome significantly predicted individual variability in speech perception in background noise (Elsabbagh et al., 2011). The deletion of 26–28 genes from chromosome 7, identified as the primary cause of Williams syndrome, may also point to the potential genetic underpinnings of efferent auditory activity (Morris, 2010).

Abnormal MEAR has been also reported in a higher proportion of introverted, socially withdrawn children and adults compared to extraverted peers, and coincides with their increased auditory sensitivity and preference for more quiet environments (Bar-Haim, 2002).

Altered MOCB function, as manifested by reduced suppression of transient evoked otoacoustic emissions, has been documented in children with autism and is thought to underlie their hypersensitivity to sound and poor speech perception in background noise (Khalfa et al., 2001; Danesh and Kaf, 2012). Children with dyslexia also showed a tendency for reduced MOCB function when compared to averagely reading control children (Veuillet et al., 2007). Moreover, MOCB function has been associated with auditory discrimination deficits of voiced–unvoiced contrasts which require phonological encoding of voice onset time duration. Interestingly, difficulty in voicing perception was proportional to the extent of reading difficulties. Learning disabled children with auditory processing disorders also showed significantly reduced suppression effect of transient evoked otoacoustic emissions and higher otoacoustic emissions amplitudes compared to controls (Muchnik et al., 2004). These authors suggest that reduced auditory inhibitory function may underlie lower MOCB activity and lead to one of the core features of auditory processing disorders, difficulties in understanding speech in background noise. Taken together, the described clinical populations exhibited auditory processing deficits along with aberrant efferent function (MEAR and/or MOCB). Importantly however, deficits in vocalization were not evident in these populations, rendering the SM population unique in this respect.

2. Abnormal auditory efferent function in SM

Consistent failure to speak in specific social situations despite the ability to speak normally in other situations is the core feature of selective mutism (American Psychiatric Association, 2013). However, although SM has been described in the medical and psychological literatures for many years (Kussmaul, 1877; Tramer, 1934), its etiology is poorly understood and the underlying neural mechanisms have only recently been explored.

Based on evidence from animals and humans regarding the involvement of efferent activity in vocalization we hypothesized that aberrant functioning of the MEAR and MOCB during vocalization in children with SM may result in distortion, excessive masking of external stimuli, and desensitization of the auditory pathway to sounds. We assumed that the ability to speak and process incoming sounds simultaneously may thus be compromised in children with SM leading to adaptation in the form of whispering, restricted vocalization, and even complete speech avoidance in situations that require highly efficient sound processing (Bar-Haim et al., 2004). Self-report of children with SM describing peculiarity in the perception of their own voice such as 'my voice sounds funny and I don't want others to hear it' (Black and Uhde, 1992) or 'my brain won't let me speak because my voice sounds strange' (Boon, 1994) provided initial anecdotal support to our conjecture.

In an attempt to test these assumptions Bar-Haim et al. (2004) studied auditory efferent and afferent function in a group of 16 children with SM compared to a group of 16 normally speaking, healthy children. All children were tested for pure-tone audiometry, speech reception thresholds, speech discrimination, MEAR thresholds and decay function, transient evoked otoacoustic emissions, suppression of transient evoked otoacoustic emissions, and auditory brainstem responses. While afferent function was intact in all children based on pure-tone audiometry, speech reception threshold, speech discrimination, and auditory brainstem response indices, aberrant auditory efferent activity was evident in the majority of children with SM. Specifically, MEAR results indicated that: (a) 50% (8/16) of the children with SM displayed no MEAR at maximum stimulation level in at least 2 of 12 assessment conditions [two ears, three tested frequencies (0.5, 1, 2 kHz), two stimulation sides (ipsi- and contra-lateral)] compared to only two children in the control group; (b) Children with SM had significantly higher prevalence of abnormal MEAR (absent or thresholds > 100 dB HL) and significantly higher MEAR thresholds for all tested frequencies excluding a marginally significant difference for right ear ipsi- and contralateral thresholds to 0.5 kHz tones; (c) Children with SM displayed significantly higher prevalence of abnormal right ear MEAR decay functions, and a marginally significant finding of higher prevalence of abnormal left ear ipsi-lateral MEAR decay function at 0.5 kHz. MOCB activity revealed that children with SM displayed significantly lower transient evoked otoacoustic emissions suppression in the right ear compared with controls. Clinical abnormality criteria of suppression effect magnitude lower than 1 dB SPL (Prasher et al., 1994) indicated significantly higher prevalence of abnormal right ear suppression in children with SM compared to controls. It should be noted, however, that due to difficulty in complying with the testing procedure transient evoked otoacoustic emissions suppression data was available from only 9 children with SM and 12 control children.

To substantiate and extend our preliminary findings of aberrant efferent function in children with SM (Bar-Haim et al., 2004) we studied an enlarged sample of 62 children, 31 with SM and 31 normally speaking, healthy children (Muchnik et al., 2013). Utilizing the same methodology, but

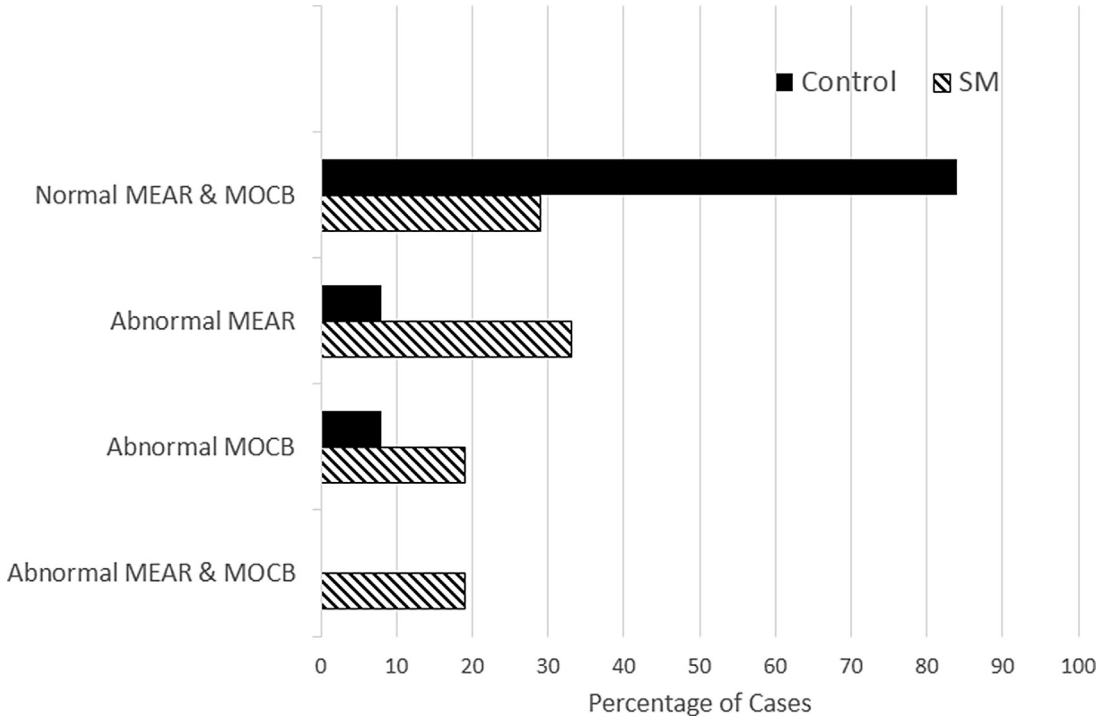

Fig. 1. The percentage of cases in the SM and control groups showing normal or abnormal MEAR function (absent MEAR and/or abnormal MEAR decay), MOCB function (reduced suppression of transient evoked otoacoustic emissions), and the combination of MEAR and MOCB.

with more stringent criteria for abnormal MEAR and MOCB, we replicated our preliminary findings of normal afferent function together with aberrant efferent function in the majority of studied children with SM. Fig. 1 depicts the percentage of cases exhibiting abnormal efferent function as demonstrated by findings of abnormal MEAR function (i.e., absent MEAR and/or abnormal MEAR decay), MOCB function (i.e., suppression of transient evoked otoacoustic emissions), and the combination of abnormal MEAR and MOCB. Analysis of data of 21 children from the SM group and 24 children from the control group with full audiological datasets indicated that 71% of the children with SM (15/21) showed abnormal findings in MEAR and/or MOCB, whereas only 16% of the control children (4/24) showed abnormal findings. The prevalence of children with SM who exhibited absent MEAR and/or abnormal MEAR decay was 59%, significantly higher than that found in the control group (10%), and similar to that reported in our preliminary study (Bar-Haim et al., 2004) despite the use of more stringent criteria for abnormal findings. No lateralization effects were evident in this enlarged sample. The prevalence of reduced MOCB function in children with SM was 38% vs. 8% in the control group. Applying the lower cut-off criterion for abnormal suppression suggested by Prasher et al. (1994) resulted in a lower prevalence rate compared to that found in our smaller cohort (58%) (Bar-Haim et al., 2004). Prevalence of abnormal findings in the healthy control group, however, was also significantly lower (8% vs. 33%, current and previous study, respectively).

Taken together, the results from Bar-Haim et al. (2004) and Muchnik et al. (2013) indicate that a proportion of children with SM exhibit aberrations in auditory efferent function. These results lead to the hypothesis that difficulty to simultaneously vocalize and process incoming sounds may underlie the aberrant speaking behavior in SM.

3. The association between aberrant auditory efferent function and self-vocalization in SM

Given the high incidence of aberrant efferent function in children with SM we opted to explore whether vocalization ability of children with SM who display abnormal auditory efferent activity differs from that of children with SM with normal efferent activity. For this purpose we designed a series of controlled single and dual tasks requiring simultaneous vocalization and auditory processing and contrasted these with corresponding visual control tasks (Arie et al., 2007). Twenty-eight children were studied: nine children with SM and abnormal efferent activity, nine children with SM and normal efferent activity, and 10 normally speaking control children. The experiment included two single-task conditions: auditory monitoring (detecting a target word in a list of spoken words) and visual monitoring (detecting a target picture in a series of pictures), and two corresponding dual-task conditions, in which a vocalization task (repeatedly counting 1–10) was added to the single-task conditions. All children were expected to show poorer performance in the dual task requiring both auditory processing and vocalization relative to the single task requiring auditory processing only. However, children with SM and with abnormal efferent activity were expected to exhibit greater decline in auditory dual-task performance

compared to children with SM who have normal auditory efferent activity and relative to healthy controls. In accord with our efferent auditory deficit hypothesis these results were expected to be specific to auditory–vocal performance, and not to visual–vocal performance.

Results indicated that children from the three groups did not differ in performance on the single auditory task. However, when required to vocalize in the dual auditory task, error rates of children with SM exhibiting abnormal auditory efferent function were significantly higher than those of children with SM exhibiting normal auditory efferent function and relative to controls. Moreover, as performance in the visual dual-task was similar among the three groups, it became clear that poorer performance in the auditory dual-task in children with SM and abnormal auditory efferent function cannot be attributed to a general difficulty in dual tasks performance.

Taken together, the results of the three studies reviewed above (Bar-Haim et al., 2004; Arie et al., 2007, Muchnik et al., 2013) appear to support the notion that MEAR and MOCB dysfunction may be associated with an auditory processing deficit in some children with SM. Difficulty in simultaneously coping with incoming sounds and self-vocalization may consciously or subconsciously challenge some children with SM with the dilemma of whether to speak, and thus jeopardize perception of incoming sounds, or listen without active vocal participation. It may be difficult to point to a consistent pattern of auditory environments and social situations in which children with SM chose to speak or to remain silent. Though speculative, it may be the case that auditory environments (e.g., school, playground) that typically involve communicating in background noise impose high perceptual demands and are therefore more prone to speech avoidance, as opposed to one-on-one scenarios at a quiet, less demanding environment (e.g., home, therapy room). Furthermore, the child's decision/ability to speak in specific situations or with specific individuals may be related to the adaptive significance assigned to the accurate processing of auditory information in that particular context. For example, it may be less taxing to miss a few words while communicating with a parent or a sibling, as opposed to answering a teacher's question while following a class discussion. The interaction between aberrant auditory efferent function and shy, socially anxious, and inhibited temperament may also affect the child's "decision" to speak or remain silent as in the case of communicating with a stranger. Clearly, additional research is warranted to clarify the enigmatic communicative behavior of children with SM.

From a developmental perspective it is important to acknowledge that the MOCB and MEAR mechanisms mature in utero or shortly after birth. Specifically, suppression of transient evoked otoacoustic emissions is observable in preterm neonates of 32–33 weeks of gestational age, reaching adult-like values at 37 weeks of gestational age (Chabert et al., 2006). Indeed, transient evoked otoacoustic emissions suppression magnitude is similar in babies (40 weeks of gestational age to 10 months), children (1–4 years), and young adults (16–20 years). Finally, similar age-related patterns were reported regarding suppression of distortion product otoacoustic emissions (Abdala et al., 2013).

Maturation of the MEAR has been studied to a lesser extent, however, extant data indicate that MEAR can be recorded from full-term neonates 48 h after birth (Vincent and Gerber, 1987; Kei, 2012) and that thresholds decrease with increasing age from 2 days to 36 weeks, at which time these thresholds become adult-like (Vincent and Gerber, 1987; Gerber et al., 1984). Thus, from a functional point of view, the MOCB and MEAR mechanisms are mature and ready to support speech and language development from the very beginning. While there is evidence for some comorbidity between SM and communication disorders including expressive and/or receptive language disorders, articulation disorders, and stuttering (Steinhausen and Juzi, 1996; Kristensen, 2000; Manassis et al., 2007; Cohan et al., 2008), the vast majority of children with SM develop normal speech and language abilities. Thus, it appears that aberrations in efferent activity are probably not the primary determinant factor of SM for most children. Instead, it is possible that for most children with SM, increased integration into the social world interacts with psychological processes and organic aberrations in the auditory efferent system to produce the clinical representation of SM. High comorbidity between SM and social anxiety may interact with auditory efferent impairments to aggravate SM symptoms and further distort auditory input. Future studies may benefit from more thorough speech and language assessments along with recordings of efferent neuro-markers in children with SM to further detail possible associations between the two. Importantly however, while formal diagnosis of speech and language was not conducted in the samples reviewed here, a clear and "normative" demonstration of speech, recorded at home on video and/or audio tapes, served as an inclusion criterion in all samples. As previously suggested, comorbid speech-language impairment should be diagnosed if the child with SM also shows these deficits when tested in non-distressing environments (e.g. home; Cohan et al., 2008). Lastly, all the children included in the reviewed articles were attending regular public schools, and did not require any special educational support, again strongly supporting normal language development (reading, writing) in the reviewed samples.

4. Preliminary findings on cortical efferent adaptation in SM

Based on the findings that some children with SM exhibit aberrant auditory efferent function at the levels of the corticofugal system projecting from the superior olivary complex to the cochlea (Bar-Haim et al., 2004; Muchnik et al., 2013), we sought to explore whether a broader deficiency in auditory suppression mechanisms is evident in higher cortically driven mechanisms (Henkin et al., 2010). We used a 'paired click paradigm' (Adler et al., 1982) to test auditory suppression in the cortex. In the 'paired click paradigm', cortical activity in response to two consecutive clicks, presented 500 msec apart, is recorded. The P50 potential elicited by the first click reflects encoding and attention processes, whereas P50 elicited by a second click, is thought to be driven by sensory gating and filtering

processes (Adler et al., 1982). Typically, healthy adults display suppressed P50 amplitude to the second click relative to the first click. Impaired P50 suppression has been associated with poor sensory gating that presumably causes an influx of irrelevant, unimportant, or distracting information that can lead to perceptual or attentional deficits (Braff and Geyer, 1990; Ghisolfi et al., 2006; Hashimoto et al., 2008; Knight et al., 1999).

Preliminary data from a group of 10 children with SM and a group of healthy, normally speaking controls indicated that cortical neural encoding of auditory information, as manifested by P50 amplitude and latency elicited by the first click, was comparable in the two groups (Henkin et al., 2010). This observation extended our previous findings of intact auditory afferent activity in SM based on auditory brainstem response recordings (Bar-Haim et al., 2004; Muchnik et al., 2013). In contrast, auditory sensory gating, as manifested by P50 suppression to the second click, differed between the groups. While children with SM exhibited mature, adult-like P50 suppression effects, control children showed highly variable responses (i.e., either suppression or augmentation) that on average did not yield a P50 suppression effect. P50 suppression was evident in 90% of the children of the SM group and only in 40% of the controls, whereas augmentation was found in 10% and 60%, respectively. Indeed, previous developmental studies in healthy children describe increase in P50 suppression effects and diminished variability with age (Brinkman and Stauder, 2007; Freedman et al., 1987; Marshall et al., 2004; Davies et al., 2009). It has been suggested that the maturational course of P50 suppression follows the maturation pattern of the frontal cortex (Brinkman and Stauder, 2007; Grunwald et al., 2003; Knight et al., 1999; Weisser et al., 2001). Children often fail to activate regions in the prefrontal cortex during tasks requiring suppression of irrelevant environmental stimuli (Bunge et al., 2002). Thus, it is plausible that the relatively large percentage of healthy children that did not show P50 suppression is related to variability in maturation of prefrontal systems that mediate auditory sensory gating. In contrast, the mature P50 suppression effect found in children with SM may presumably reflect a cortical mechanism of compensatory inhibition of irrelevant auditory information that was not properly suppressed at the brainstem level (Henkin et al., 2010). We therefore speculate that it may be the case that diminished efferent activity at the brainstem level spurs early maturation of the P50 suppression effect in some children with SM.

5. Potential implications for treatment

Over the past decade SM has been typically conceptualized as an anxiety disorder (Beidel & Turner, 2005; Viana et al., 2009). Some researchers and clinicians suggested that SM is in fact an extreme type of social anxiety disorder (Black and Uhde, 1992, 1995). Alternatively it is conceivable that vocalizing, in and of its own, may constitute the feared context as in specific phobias. Both lines of clinical thought lead to cognitive behavior therapy (CBT) and selective serotonin reuptake inhibitors (SSRIs) gaining center stage as first-line treatments for SM, with both approaches showing limited success (Kaakeh and Stumpf, 2008; Keeton and Budinger, 2012). While there are some indications for the involvement of Serotonin in auditory processing (Gopal et al., 2000; Thompson et al., 1998), the primary neurotransmitter supporting inhibitory efferent activity at the olivocochlear bundle and in the neuromuscular junction responsible for activation of the MEAR is acetylcholine (Godfrey et al., 1990; Simmons, 2002). Thus, current pharmacological and psychological treatments may not be able to target the underling auditory efferent deficits exhibited by a considerable portion of children with SM. The clinical efficacy of current treatments will probably remain limited to the anxiety symptoms commonly found in children with SM, leaving the speech-related primary symptom of the disorder untreated.

Future therapies for SM may wish to attempt direct targeting of the auditory deficiencies outlined in the current report, either in addition to the standard psychological and pharmaceutical treatments or as standalone treatments. Indeed, recent years have witnessed an increase in neuroscience-based therapeutic targeting of specific perceptual and cognitive deficits (e.g., Pine et al., 2009; Bar-Haim, 2010; Bar-Haim and Pine, 2013). One relevant example is work by Tallal and colleagues (1996) revealing how understanding neural dynamics of auditory processing during speech perception and language comprehension has led to the development of neuroplasticity-based intervention strategies aimed at ameliorating language and literacy problems. As abnormal efferent function can be documented non-invasively by means of reliable and accurate clinical audiological tools, children with SM could be tested and their specific auditory deficits could then be treated. Children with auditory processing disorders, for example, have been offered deficit-specific training protocols in an attempt to stimulate neuroplasticity in auditory pathways, with some success (e.g., Bellis, 2003; Moncrieff and Wertz, 2008). For children with SM, graded exposure to one's own voice via headphones, subsequent addition of background noise, and simulation of speech in social situations precipitating the speech-avoidance behavior, may facilitate auditory processing during vocalization, and ameliorate communicative dysfunction. Additionally, computerized protocols could be designed to induce gradual improvement in vocalizing-listening dual tasks in children with SM.

In parallel, future neurochemical and neuroimaging research on the human auditory efferent system could reveal specific targets for pharmacological and non-invasive brain stimulation techniques for SM. Possibly, inhibitory and excitatory repetitive transcranial magnetic stimulation (rTMS) or transcranial direct current stimulation (tDCS) could be applied in combination with behavioral tasks to ameliorate SM symptoms. For instance, some research has shown promise for such non-invasive stimulation in the neuro-rehabilitation of communication disorders such as post-stroke aphasia (Shah et al., 2013).

Functionality of the auditory efferent system can be assessed reliably and non-invasively right after birth, a fact that could have important implications for timing of implementing prevention or intervention strategies for toddlers at-risk for SM. However, such implementation hinges on

good understanding of the developmental time course of SM, which is currently largely lacking. SM's age at onset has been reported to range from 2.7 to 4.1 years (See Viana et al., 2009). However, SM may go unrecognized until the child is consistently confronted with challenges of speaking in specific social situations leading to a substantial lag between onset of the disorder and time of referral. For example, in one of the only controlled studies on outcome of SM, the mean age at referral for treatment was 8.5 years (Steinhausen et al., 2006). If early efferent auditory neuro-markers of risk could be identified before the onset of SM, then early interventions targeting the neural underpinnings as well as early signs of social reticence could circumvent the negative trajectory of the disorder. Similar reasoning has been applied to other developmental disorders such as autism (e.g., Woods and Wetherby, 2003).

In summary, growing evidence suggest substantial involvement of auditory efferent activity during vocalization in the psychopathology of some children with SM. In a series of studies, SM, a rare and behaviorally perplexing condition in which vocalization is selectively compromised, served as a human model for the investigation of auditory efferent involvement in vocalization. Data indicate aberrant efferent activity in a large proportion of children with SM that may underlie deficient auditory processing during vocalization in these children. These auditory aberrations appear to impair the ability of some children with SM to simultaneously speak and process incoming auditory information. Perhaps, when some children with SM are faced with the negative consequences of vocalization on their capacity to process external incoming sounds they adapt by restricting and avoiding speech. This possibility points to novel intervention options for this chronic and difficult to treat disorder, which if applied early in development, before children emerge into the more complex social world, could circumvent the outbreak and chronic course of SM. Additional research is needed to further elucidate the exact nature of the interplay between aberrant efferent auditory function and psychological and behavioral aspects of the disorder. Furthermore, developmental research on recovery or partial recovery from SM and its relation to auditory neural function could shed light on the clinical course of the disorder.

Conflict of interest

The authors declare that the current research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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References

Abdala, C., Mishra, S., Garinis, A., 2013. Maturation of the human medial efferent reflex revisited. J. Acoust. Soc. Am. 133, 938–950.

Adler, L.E., Pachtman, E., Franks, R.D., Pecevich, M., Waldo, M.C., Freedman, R., 1982. Neurophysiological evidence for a defect in neuronal mechanisms involved in sensory gating in schizophrenia. Biol. Psychiatry 17, 639–654.

American Psychiatric Association, 2013. Diagnostic and Statistical Manual of Mental Disorders, 5th ed. American Psychiatric Publishing, Arlington, VA.

Arie, M., Henkin, Y., Lamy, D., Tetin-Schneider, S., Apter, A., Sadeh, A., et al., 2007. Reduced auditory processing capacity during vocalization in children with selective mutism. Biol. Psychiatry 61, 419–421.

Bar-Haim, Y., 2002. Introversion and individual differences in acoustic reflex function. Int. J. Psychophysiol. 46, 1–11.

Bar-Haim, Y., Henkin, Y., Ari-Even-Roth, D., Tatin-Schneider, S., Hildesheimer, M., Muchnik, C., 2004. Reduced auditory efferent activity in childhood selective mutism. Biol. Psychiatry 55, 1061–1068.

Bar-Haim, Y., 2010. Attention Bias Modification (ABM): a novel treatment for anxiety disorders. J. Child Psychol. Psychiatry 51, 859–870.

Bar-Haim, Y., Pine, D.S., 2013. Cognitive training research and the search for a transformative, translational, developmental cognitive neuroscience. Dev. Cogn. Neurosci. 4, 1–2.

Beidel, D.C., Turner, S.M., 2005. Childhood Anxiety Disorders: A Guide to Research and Treatment. Taylor and Francis, New York.

Bellis, T.J., 2003. Assessment and Management of Central Auditory Processing Disorders in the Educational Setting, From Science to Practice, 2nd ed. Thomson Delmar Learning, Clifton Park.

Bergman, R.L., Piacentini, J., McCrocken, J.T., 2002. Prevalence and description of selective mutism in a school-based sample. J. Am. Acad. Child Adolesc. Psychiatry 41, 938–946.

Black, B., Uhde, T.W., 1992. Elective mutism as a variant of social phobia. J. Am. Acad. Child Adolesc. Psychiatry 31, 1090–1094.

Black, B., Uhde, T.W., 1995. Psychiatric characteristics of children with selective mutism: pilot study. J. Am. Acad. Child Adolesc. Psychiatry 34, 847–856.

Blomberg, S., Rosander, M., Andersson, G., 2006. Fears, hyperacusis and musicality in Williams syndrome. Res. Dev. Disabil. 27, 668–680.

Borg, E., Zakrisson, J.E., 1975. The activity of the stapedius muscle in man during vocalization. Acta Otolaryngol. 79, 325–333.

Borg, E., Counter, S.A., 1989. The middle-ear muscles. Sci. Am. 260, 74–80.

Borg, E., Bergkvist, C., Gustafsson, D., 2009. Self-masking: listening during vocalization. Normal hearing. J. Acoust. Soc. Am. 25, 3871–3881.

Boon, F., 1994. The selective mutism controversy (continued). J. Am. Acad. Child Adolesc. Psychiatry 33 (2), 283.

Braff, D.L., Geyer, M.A., 1990. Sensorimotor gating and schizophrenia. Human and animal model studies. Arch. Gen. Psychiatry 47, 181–188.

Brinkman, M.J.R., Stauder, J.E.A., 2007. Development and gender in the P50 paradigm. Clin. Neurophysiol. 118, 1517–1524.

Brown, G.J., Ferry, R.T., Meddis, R., 2010. A computer model of auditory efferent suppression: implications for the recognition of speech in noise. J. Acoust. Soc. Am. 127, 943–954.

Bunge, S.A., Dudukovic, N.M., Thomason, M.E., Vaidya, C.J., Gabrieli, J.D., 2002. Immature frontal lobe contributions to cognitive control in children: evidence from fMRI. Neuron 33, 301–311.

Cunningham, C.E., McHolm, A., Boyle, M.H., Pate, P., 2004. Behavioral and emotional adjustment, family functioning, academic performance, and social relationships in children with selective mutism. J. Child Psychol. Psychiatry 45, 1363–1372.

Chabert, R., Guitton, M.J., Amram, D., Uziel, A., Pujol, R., Lallemant, J., Puel, J., 2006. Early maturation of evoked otoacoustic emissions and medial olivocochlear reflex in preterm neonates. Pediatr. Res. 59, 305–308.

Cohan, S.L., Chavira, D.A., Shipon-Blum, E., Hitchcock, C., Roesch, S.C., Stein, M.B., 2008. Refining the classification of children with selective mutism: a latent profile analysis. J. Clin. Child Adolesc. Psychol. 37, 770–784.

Cooper, N.P., Guinan Jr., J.J., 2006. Efferent-mediated control of basilar membrane motion. J. Physiol. 576, 49–54.

Collet, L., Kemp, D.T., Veuillet, E., Duclaux, R., Moulin, A., Morgon, A., 1990. Effects of contralateral auditory stimuli on active cochlear micro-mechanical properties in human subjects. Hear. Res. 43, 251–262.

Curio, G., Neuloh, G., Numminen, J., Jousmaki, V., Hari, R., 2000. Speaking modifies voice-evoked activity in the human auditory cortex. Hum. Brain Mapp. 9, 183–191.

Danesh, A.A., Kaf, W.A., 2012. DPOAEs and contralateral acoustic stimulation and their link to sound hypersensitivity in children with autism. Int. J. Audiol. 51, 345–352.

Davies, P.L., Chang, W., Gavin, W.J., 2009. Maturation of sensory gating performance in children with and without sensory processing disorders. Int. J. Psychophysiol. 72, 187–197.

Doupe, A.J., Kuhl, P.K., 1999. Birdsong and human speech: common themes and mechanisms. Annu. Rev. Neurosci. 22, 567–631.

Elsabbagh, M., Cohen, H., Cohen, M., Rosen, S., Karmiloff-Smith, A., 2011. Severity of hyperacusis predicts individual differences in speech perception in Williams syndrome. J. Intellect. Disabil. Res. 55, 563–571.
Freedman, R., Adler, L.E., Walso, M.C., 1987. Gating of the auditory evoked potential in children and adults. Child Dev. 24, 223–227.
Gerber, S.E., Gong, E.L., Mendel, M.I., 1984. Developmental norms for the acoustic reflex. Audiology 23, 1–8.
Ghisolfi, E.S., Heldt, E., Zanardo, A.P., Strimitzer Jr., I.M., Prokopiuk, A.S., Becker, J., et al., 2006. P50 sensory gating in panic disorder. J. Psychiatr. Res. 40, 535–540.
Giraud, A.L., Garnier, S., Micheyl, C., Lina, G., Chays, A., Chery-Croze, S., 1997. Auditory efferents involved in speech-in-noise intelligibility. Neuroreport 8, 1779–1783.
Godfrey, D.A., Wiet, G.J., Parli, J.A., Beranek, K.L., Ross, C.D., 1990. Enzymes of transmitter and energy metabolism in rat middle ear and extraocular muscles. Hear. Res. 48, 187–194.
Goldberg, R.L., Henson Jr., O.W., 1998. Changes in cochlear mechanics during vocalization: evidence for a phasic medial efferent effect. Hear. Res. 22, 71–81.
Gopal, K.V., Daly, D.M., Daniloff, R.G., Pennartz, L., 2000. Effects of selective serotonin reuptake inhibitors on auditory processing: a case study. J. Am. Acad. Audiol. 11, 454–463.
Gothelf, D., Ferber, N., Raveh, E., Apter, A., Attias, J., 2006. Hyperacusis in Williams syndrome: characteristics and associated neuroaudiologic abnormalities. Neurology 66, 390–395.
Grunwald, T., Boutros, N.N., Pezer, N., von Oertzen, J., Fernández, G., Schaller, C., et al., 2003. Neuronal substrates of sensory gating within the human brain. Biol. Psychiatry 53, 511–519.
Guinan Jr., J.J., 2006. Olivocochlear efferents: anatomy, physiology, function, and the measurement of efferent effects in humans. Ear Hear. 27, 589–607.
Guinan Jr., J.J., 2010. Cochlear efferent innervation and function. Curr. Opin. Otolaryngol. Head Neck Surg. 18, 447–453.
Hashimoto, T., Shimizu, E., Koike, K., Orita, Y., Suzuki, T., Kanahara, N., et al., 2008. Deficits in auditory P50 inhibition in obsessive-compulsive disorder. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 32, 288–296.
Henkin, Y., Feinholz, M., Arie, M., Bar-Haim, Y., 2010. P50 suppression in children with selective mutism: a preliminary report. J. Abnorm. Child Psychol. 38, 43–48.
Hoy, R., 2002. Tuning in by tuning off. Nature 418, 831–833.
Kaakeh, Y., Stumpf, J.L., 2008. Treatment of selective mutism: focus on selective serotonin reuptake inhibitors. Pharmacotherapy 28, 214–224.
Keeton, C.P., Budinger, M.C., 2012. Social phobia and selective mutism. Child Adolesc. Psychiatr. Clin. N. Am. 21, 621–641.
Kei, J., 2012. Acoustic stapedial reflexes in healthy neonates: normative data and test–retest reliability. J. Am. Acad. Audiol. 23, 46–56.
Khalfa, S., Bruneau, N., Roge, B., Georgieff, N., Veuillet, E., Adrien, J.C., et al., 2001. Peripheral auditory asymmetry in infantile autism. Eur. J. Neurosci. 13, 628–632.
Knight, R.T., Staines, W.R., Swick, D., Chao, L.L., 1999. Prefrontal cortex regulates inhibition and excitation in distributed neural networks. Acta. Psychol. (Amst) 101, 159–178.
Kristensen, H., 2000. Selective mutism and comorbidity with developmental disorder/delay, anxiety disorder, and elimination disorder. J. Am. Acad. Child Adolesc. Psychiatry 39, 249–256.
Kumar, U.A., Vanaja, C.S., 2004. Functioning of olivocochlear bundle and speech perception in noise. Ear Hear. 25, 142–146.
Kussmaul, A., 1877. Die Storungen der Sprache. FCW Vogel, Leipzig.
Lee, B.S., 1950. Effects of delayed speech feedback. J. Acoust. Soc. Am. 22, 824–826.
Lamprecht, A., 1988. Changes of the voice in the Lombard reflex. Laryngol. Rhinol. Otol. 67, 350–354.
Maison, S.F., Usubuchi, H., Liberman, M.C., 2013. Efferent feedback minimizes cochlear neuropathy from moderate noise exposure. J. Neurosci. 33, 5542–5552.
Manassis, K., Fung, D., Tannock, R., Sloman, L., Fiksenbaum, L., McInnes, A., 2003. Characterizing selective mutism: is it more than social anxiety? Depress. Anxiety 18, 153–161.
Manassis, K., Tannock, R., Garland, E.J., Minde, K., McInnes, A., Clark, S., 2007. The sounds of silence: language, cognition, and anxiety in selective mutism. J. Am. Acad. Child Adolesc. Psychiatry 46, 1187–1195.
Marshall, P.J., Bar-Haim, Y., Fox, N.A., 2004. The development of P50 suppression in the auditory event-related potential. Int. J. Psychophysiol. 51, 135–141.
Messing, D.P., Delhorne, L., Bruckert, E., Braida, L.D., Ghitza, O., 2009. A non-linear efferent-inspired model of the auditory system; matching human confusions in stationary noise. Speech Commun. 51, 668–683.
Micheyl, C., Collet, L., 1996. Involvement of olivocochlear bundle in the detection of tones in noise. J. Acoust. Soc. Am. 99, 1604–1610.
Micheyl, C., Perrot, X., Collet, L., 1997. Relationship between auditory intensity discrimination in noise and olivocochlear efferent system activity in humans. Behav. Neurosci. 3, 801–807.
Moncrieff, D.W., Wertz, D., 2008. Auditory rehabilitation for interaural asymmetry: preliminary evidence of improved dichotic listening performance following intensive training. Int. J. Audiol. 47, 84–97.
Morris, C.A., 2010. The behavioral phenotype of Williams syndrome: a recognizable pattern of neurodevelopment. Am. J. Med. Genet. 154C, 427–431.
Muchnik, C., Ari-Even Roth, D., Othman-Jebara, R., Putter-Katz, H., Shabtai, E., Hildesheimer, M., 2004. Reduced medial olivocochlear bundle system function in children with auditory processing disorders. Audiol. Neurotol. 9, 107–114.
Muchnik, C., Ari-Even Roth, D., Hildesheimer, M., Arie, M., Bar-Haim, Y., Henkin, Y., 2013. Abnormalities in auditory efferent activities in children with selective mutism. Audiol. Neurootol. 18, 353–361.
Oller, D.K., Eilers, R.E., 1988. The role of audition in infant babbling. Child Dev. 59, 441–449.
Osmanski, M.S., Dooling, R.J., 2009. The effect of altered auditory feedback on control of vocal production in budgerigars (*Melopsittacus undulatus*). J. Acoust. Soc. Am. 126, 911–919.
Pine, D.S., Helfenstein, S., Bar-Haim, Y., Nelson, E., Fox, N.A., 2009. Challenges in the development of novel therapeutics for the treatment of childhood central nervous system disorders. Neuropsychopharmacology 34, 213–228.
Poulet, J., Hedwig, B., 2002. A corollary discharge maintains auditory sensitivity during sound production. Nature 418, 872–876.
Prasher, D., Ryan, S., Luxon, L., 1994. Contralateral suppression of transient evoked otoacoustic emissions and neuro-otology. Br. J. Audiol. 28, 247–254.
Robertson, D., 2009. Centrifugal control in mammalian hearing. Clin. Exp. Pharmacol. Physiol. 36, 603–611.
Shah, P.P., Szaflarski, J.P., Allendorfer, J., Hamilton, R.H., 2013. Induction of neuroplasticity and recovery in post-stroke aphasia by non-invasive brain stimulation. Front. Hum. Neurosci. 7, 1–17.
Simmons, D.D., 2002. Development of the inner ear efferent system across vertebrate species. J. Neurobiol. 53, 228–250.
Steinhausen, H.C., Juzi, C., 1996. Elective mutism: an analysis of 100 cases. J. Am. Acad. Child Adolesc. Psychiatry 35, 606–614.
Steinhausen, H.C., Wachter, M., Laimbock, K., Metzke, C.W., 2006. A long-term outcome study of selective mutism in childhood. J. Child Psychol. Psychiatry 47, 751–756.
Suga, N., Jen, P.H., 1975. Peripheral control of acoustic signals in the auditory system of echo locating bats. J. Exp. Biol. 62, 277–311.
Tallal, P., Miller, S.L., Bedi, G., Byma, G., Wang, S., Nagarajan, S.S., et al., 1996. Language comprehension in language-learning impaired children improved with acoustically modified speech. Science 271, 81–84.
Thompson, A.M., Thompson, G.C., Britton, B.H., 1998. Serotoninergic innervation of stapedial and tensor tympani motoneurons. Brain Res. 787, 175–178.
Tramer, M., 1934. Elektiver Mutismus bei Kindern. Z Kinderpsychiatr. 1, 30–35.
Ventura, M.I., Nagarajan, S.S., Houde, J.F., 2009. Speech target modulates speaking induced suppression in auditory cortex. BMC Neurosci. 10, 58–68.
Veuillet, E., Magnan, A., Ecalle, J., Thai-Van, H., Collet, L., 2007. Auditory processing disorder in children with reading disabilities: effect of audiovisual training. Brain 130, 2915–2928.
Viana, A.G., Beidel, D.C., Rabian, B., 2009. Selective mutism: a review and integration of the last 15 years. Clin. Psychol. Rev. 29, 57–67.
Vincent, L.V., Gerber, S.E., 1987. Early development of the acoustic reflex. Audiology 26, 356–362.
Weisser, R., Weisbrod, M., Roehrig, M., Rupp, A., Schroeder, J., Scherg, M., 2001. Is frontal lobe involved in the generation of the auditory evoked P50? Neuroreport 12, 3303–3307.
Woods, J.J., Wetherby, A.M., 2003. Early identification of and intervention for infants and toddlers who are at risk for autism spectrum disorder. Lang. Speech Hear. Serv. Sch. 34, 180–193.
Xie, D.H., Henson Jr., O.W., 1998. Tonic efferent-induced cochlear damping in roosting and echolocating mustached bats. Hear. Res. 124, 60–68.
Yeganeh, R., Beidel, D.C., Turner, S.M., Pina, A.A., Silverman, W.K., 2003. Clinical distinctions between selective mutism and social phobia: an investigation of childhood psychopathology. J. Am. Acad. Child Adolesc. Psychiatry 42, 1069–1075.