Effect of mechanical tactile noise on the amplitude of visual evoked potentials: Multisensory stochastic resonance

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Abstract

The present investigation documents the electrophysiological occurrence of multisensory stochastic resonance in the human visual pathway elicited by tactile noise. We define multisensory stochastic resonance of brain evoked potentials as the phenomenon in which an intermediate level of input noise of one sensory modality enhances the brain evoked response of another sensory modality. Here we examined this phenomenon in visual evoked potentials (VEP) modulated by the addition of tactile noise. Specifically, we examined whether a particular level of mechanical Gaussian noise applied to the index finger can improve the amplitude of the VEP. We compared the amplitude of the positive P100 VEP component between zero noise (ZN), optimal noise (ON) and high mechanical noise (HN). The data disclosed an inverted U-like graph for all the subjects, thus demonstrating the occurrence of a multisensory stochastic resonance in the P100 VEP.

Keywords: Tactile noise; Stochastic resonance; Cross-modal stochastic resonance; Visual; Multisensory stochastic resonance.
Stochastic resonance (SR) is a phenomenon in which an intermediate level of noise enhances the response of a nonlinear system to a weak input signal (Benzi et al., 1981; Douglass et al., 1993; Longtin et al., 1993; Wiesenfeld et al., 1995; Pei et al., 1996; Lindner et al., 2004). Typically, the amplitude of the nonlinear response versus the input noise is an inverted U-like function characterized by maximal enhancement of the response at a specific noise amplitude value. SR type effects have been demonstrated in physical and biological systems (Moss et al., 2004). Commonly, SR has been studied in diverse sensory systems in which the signal and noise applied were of the same sensory modality (Segundo et al., 1994; Collins et al., 1996; Simonotto et al., 1997; Winterer et al., 1999; Zeng et al., 2000; Lindner et al., 2004; Long et al., 2004; Mori and Kai 2002; Manjarrez et al., 2002, 2003; Aihara et al., 2010); however, there are few studies addressing the influence of noise within one sensory modality on the responses elicited by stimuli of another modality. The purpose of the present study was to analyze changes in the amplitude of the visual evoked potentials (VEP) when a continuous tactile noise was applied on the index finger. We assume that tactile inputs could produce an impact on visual perception. This idea was based on a previous report by Deibert et al., 1999 (see also Amedi et al., 2002), who employed functional magnetic resonance to demonstrate that visual cortical areas are also active during tactile object recognition. In fact there is evidence about mechanisms of tactile integration that are analogous to those related to visual processing (Bensmaia et al., 2006; Pei et al., 2011), thus suggesting an integration...
between both modalities. We also assume that in the central nervous system there are multisensory neurons participating in the tactile-visual cross-modal integration of the signal and noise inputs (Barth and Brett-Green 2004; Stein et al., 1988; Stein et al., 1996; Stein and Meredith 1993; Stein et al., 1993; Wallace et al., 1992; Kadunce et al., 1997; Calvert and Lewis 2004; Collins et al., 2005; Gentile et al., 2011). Based on the above-mentioned studies we define multisensory stochastic resonance of brain evoked potentials as the phenomenon in which an intermediate input noise level of one sensory modality enhances the brain evoked response of another sensory modality.

To our knowledge the first description about the psychophysical effect of tactile noise on visual perception was given by Lugo et al. (2012). The authors demonstrated that tactile noise is capable of decreasing luminance modulated thresholds. They employed a psychophysical paradigm in which the activity created by the interaction of the excitatory signal (visual input) and the facilitating signal (tactile noise) at some specific energy, produces the capability for a central detection of an otherwise weak signal.

In a general context our study also supports previous findings about psychophysical multisensory stochastic resonance in other sensory modalities (Manjarrez et al., 2007; Lugo et al., 2008a). For example, Lugo et al., 2008a demonstrated that auditory noise facilitates tactile, visual and proprioceptive sensations via cross-modal stochastic resonance, showing that this phenomenon is a ubiquitous property in psychophysical experiments in humans. These findings were consistent with parallel studies about psychophysical multisensory integration.
of tactile-auditory and tactile-visual interactions in which the central nervous system modulates the peripheral sensory inputs (Lugo et al., 2008b). Previous studies about multisensory stochastic resonance in the auditory-visual interactions were published in abstract form (Faubert et al., 2007; Mendez-Balbuena et al., 2014) or in subsequent articles (Manjarrez et al., 2007; Lugo et al., 2008a; Gleiss and Kayser, 2014). Consistent with these findings, Ross et al., 2008 showed that the listener's ability to understand spoken words from the observation of other person performing mouth articulatory movements is improved during noisy environmental conditions. Recently, Liu et al. (2013) confirmed that this type of audio-visual speech recognition reflects a multisensory stochastic resonance.

In our recent studies, we demonstrated that an optimum level of tactile noise applied on the finger can improve the performance of a visuomotor task in which the subjects had to compensate isometrically a target force in order to keep a visual feedback (Mendez-Balbuena et al., 2012; Trenado et al., 2014a). A question derived from these studies is whether a multisensory stochastic resonance in the visual and tactile modalities is also involved. The purpose of the present study was to address this question and extend our previous experiments, only this time, employing a paradigm of multisensory stochastic resonance. The electrophysiological experiments we performed also extend the recent psychophysical study by Lugo et al., (2012) that dealt with the effects of tactile noise on the multisensory integration of visual signals. Specifically, our study contributes in understanding visuotactile information processing via multisensory SR within the central nervous system in the context of electrophysiological signals.
**Materials and Methods**

**Subjects**

Eight healthy right-handed subjects (5 females and 3 males, 22-42 years of age; mean age 29.6 ± 6.2 years) without any history of neurological disease took part in the study. We employed a sample of eight subjects, as in our previous study (Mendez-Balbuena et al., 2012) because the results obtained here were also clear and consistent within and across subjects. To exclude cyclic ovarian effects on the cortical excitability and oscillatory cortical activity, the female subjects were in different lunar phases (Smith et al., 2002). The handedness was tested according to the Oldfield questionnaire (Oldfield 1971). All subjects participated according to the declaration of Helsinki established by the World Medical Association, with understanding and informed consent for each subject and approval of the local ethics committee from the Institute of Physiology of the Benemérita Universidad Autónoma de Puebla, México.

**Experimental Paradigm**

**Visual stimulation**

During the experimental session, the subjects sat comfortably in an electrically shielded dimly lit room. The visual stimuli consisted of a visual pattern-reversal task (8x8 checkerboard pattern with a cross as a fixation point; 32 white and 32 black rectangles, size: 6 cm x 3.5 cm; the pattern reverses every half-second) delivered by the NeuroScan Stim (v.3.0) system. The subjects were instructed to avoid any other movements and to fix their gaze on the centre of the
monitor (cross). The subjects viewed the reversal checkerboard at 1 meter distance. We selected the 8x8 rectangle-checkerboard because it produced P100 VEPs with amplitude of about 40% of the maximal P100 VEPs amplitude which was elicited with 32x32 rectangles (Figure 1). The third circle in Figure 1D indicates the type of evoked responses we employed for our experiments with the addition of tactile noise applied to the right index finger (see next sections). This shows that the P100 VEPs of this amplitude elicited by the 8x8 checkerboard are not saturated and therefore they could be incremented or decremented by the addition of tactile noise.

It is interesting to mention that the origin of the P100 component is controversial (see table 1 in Di Russo et al., 2005). Some investigators suggest that the P100 is mainly generated in extrastriate visual areas, while the majority has proposed that the P100 is generated (like the N75) in the striate area of the occipital cortex. Furthermore, the P100 VEP component has been implicated as a neural correlate of selective focal attention (Mangun and Hillyar, 1990; Luck et al., 1993; Heinze et al., 1994; Di Russo and Spinelli, 1999).

**Tactile stimulation**

The tactile stimulus was applied to the glabrous skin of the medial portion of the right index fingertip. The right hand of each subject was held in a fixed position and a 1 mm diameter flat cylindrical probe of acrylic was used to apply tactile stimuli on the finger. The tactile stimulation consisted of broad-band Gaussian noise (from 0 to 5 mN; 0-200 Hz) (Figure 2A). This noise stimulation was applied to the subject’s finger superimposed upon a constant indentation force offset of 0.1 N. We employed this broad-band noise because in a previous study we demonstrated
that it produces stronger SR effects (Trenado et al., 2014a). The output of a noise
generator (Wavetek, San Diego, CA, 132) provided input to a closed-loop
mechanical stimulator-transducer (Chubbuck, 1966), that allowed measurements
of the force and displacement of the applied stimuli. This method of tactile
stimulation was previously reported by our laboratory (Manjarrez et al., 2002;
2003).

The experimental paradigm: Cross-modal stimulation

Figure 2 shows the whole experimental scheme with the visual signal and
tactile noise stimuli. Each “set of trials” consisted of a sequence of 90 trials. We
maintained the intensity of the continuous tactile input noise constant for each “set
of trials” and varied it between them in randomized order. We applied six different
tactile noise intensity levels (from 0 to 5 mN). The resting interval between every
trial was 5 s. We delivered the same level of noise across the set of 90 trials
because we employed an analog noise stimulator; however, we suggest that
similar results could be found if the experimental paradigm consists of randomized
noise levels across trials delivered via software and a digital-to-analog converter.

As data specifying the level of noise that induces multisensory visual
stochastic resonance in the occipital lobe is not existing in the literature, first we
explored the optimum noise level that produced an increase in the P100 VEP
amplitude. We defined optimum noise (ON) as the intermediate noise level applied
on the finger that produces the maximum increase in the amplitude of the positive
P100 VEP component in comparison to zero noise (ZN). Moreover, high noise
(HN) was defined as the noise level which produces a significant decrease of the P100 VEP amplitude in comparison to ON.

**Recordings of VEP during the cross-modal stimulation**

Electroencephalographic (EEG) signals (bandpass DC-200 Hz, sampling rate 2000 Hz) were recorded from O1, OZ, O2 and C3 channels, referenced to the ear lobes, with ground at the forehead according to the 10/20 system (SynAmps, NeuroScan, El Paso, TX) (Figure 2). Electrodes impedances were kept under 5 kOhm. The electrooculogram (same bandpass and sampling rate as for EEG) was recorded to exclude trials contaminated with eye movements for further analysis.

Tactile noise (sensed in a scale of mN by the Chubbuck stimulator transducer) was simultaneously recorded with the electrophysiological data in an additional SynAmps channel of high level input (same bandpass and sampling rate as for EEG). Furthermore, the trigger of the pattern reversal checkerboard was simultaneously stored for averaging. All data were stored and analyzed off-line to obtain the averaged VEPs during the different levels of tactile noise.

**Data analysis**

**P100 VEP amplitude during cross-modal stimulation**

The whole data set recorded during the application of the six levels of tactile noise was included for further analysis. VEP’s were averaged from 60 artifact-free recordings off line by using the commercial software “Brain Vision 2.0.1” (München, Germany). We defined the P100 VEP amplitude as the absolute value
of the difference between the larger positive amplitude component (i.e., P100 component occurring at approximately 100ms) and the base line (Figure 2F).

**Statistical Analysis**

To test for any statistical difference in the P100 VEP amplitude between conditions ZN, ON and HN, we considered prominent P100 VEP peaks for each condition. Because we wanted to compare the conditions ZN vs. ON, HN vs. ON and ZN vs. HN, we performed statistical analysis on the P100 VEP amplitude related to these three noise levels. Because our data were normally distributed (Kolmogorov–Smirnov normality test, p>0.05) and had homogeneity of variances (Levene test, p>0.05) we used a parametric one-way repeated-measures ANOVA, under the null hypothesis that the dependent variables were the same across these three conditions. Moreover, Mauchly’s test indicated that the assumption of sphericity was not violated. We performed a pairwise post hoc test, using a corrected Bonferroni adjustment. All effects are reported as significant if p < 0.01.

**Results**

No subjects reported any fatigue or anxiety during the experimental sessions.

**Effects of the tactile noise on the amplitude of P100 VEP**

In the present study we found that an individually determined optimal noise level (0-200 Hz) applied to the right-index finger increased the amplitude of the P100 VEP, which was elicited by the pattern-reversal stimuli. The level of vibrotactile noise inducing multisensory SR varied between 0.1 and 5 mN. ON and HN were defined for each subject. Therefore the noise magnitude applied was
different across subjects. Table 1 shows the actual values of tactile ON and HN used across subjects.

In order to demonstrate that cross-modal interactions did not produce habituation we calculated the VEP P100 amplitude over 3 blocks of 20 trials to complete 60 clean trials (of 90 trials) in a given level of noise. Moreover, we compared changes in such amplitudes during ZN (the control), ON and HN. We found that there are not significant differences (p > 0.05; one-way repeated-measures ANOVA) in the time course of the VEP P100 amplitudes between HN, ON and ZN. This finding could be explained by the fact that we are only applying 90 visual presentations of the pattern reversal. Most of the studies that analyze VEP habituation employ more sets (blocks) of visual presentations (about 6 blocks of 100 trials) to detect VEP P100 habituation (eg., see Figure 2 in Coppola et al., 2010).

Figure 3 illustrates averaged recordings of the VEPs in the three conditions (ZN, ON and HN) for all the subjects. For all subjects (S1 to S8), the highest amplitude of the VEP P100 occurred over the primary visual cortex particularly at OZ (4/8), O1 (2/8), and O2 (2/8). Note that the P100 component of the VEP was increased during the ON condition for all the subjects. Because only the P100 component of the VEP exhibited clear changes due to the application of ON to the right-index finger, this was the only component considered for statistical analysis.

Figure 4 shows the statistical analysis for the amplitude of the P100 VEP components illustrated in Figure 3. All the subjects (8/8) exhibited an inverted U-
like curve corresponding to the amplitude of the P100 VEP as a function of the input tactile noise level. Moreover, they clearly showed inter-individual differences in the amplitude of the P100 VEP (Figure 4A). The qualitative description of these curves may apply to all. As the noise amplitude increases, the amplitude of P100 VEP becomes larger till it reaches a maximum, namely the slope (growth) becomes zero within a particular interval of noise amplitudes. After reaching this peak, under higher noise amplitudes, the curve subsides gradually and the slope (growth) becomes negative. The percentage of change for the grand average of the P100 VEP amplitude (ON versus ZN) for all subjects was $50.7 \pm 9.7 \%$ (mean ± SE). Figure 4B shows the existence of an ON level for which the P100 VEP amplitude reaches a maximum.

We performed the parametric one-way repeated-measures ANOVA to examine the statistical significance of the change in the P100 VEP amplitude, between the three conditions (ON, ZN and HN) in all eight subjects. The results showed significant differences between the three conditions ($F(2,14)=52.2, **$, $p<0.001$). The post hoc test, indicated that the significant main effect reflected significant differences between ZN and ON ($p < 0.001$) and between ON and HN ($p < 0.001$). In contrast, no statistically significant differences were found between conditions ZN and HN.

To verify that the noisy mechanical stimuli do not elicit SR-type behaviours in other brain areas that conceivably are not responsive with a P100 relative to the visual stimuli, we performed an identical analysis on the signals recorded from the C3 electrode placed on the region overlying the somatosensory area (Figure 5). In
this region, we did not observe P100 evoked responses to the visual stimuli like those observed in O1, Oz or O2. Furthermore, for these C3 recordings we did not observe evidence of SR type behaviour in the plots obtained for all the subjects (Figure 6). In summary, for the region C3, the parametric one-way repeated-measures ANOVA test showed no significant differences between the three conditions (ZN, ON and HN, p>0.05).

We performed time-frequency analysis for the grand-average of visual evoked potentials from -300 to +200 ms, time-locked to stimulus onset at 0 ms. Figure 7 illustrates the results of this time-frequency analysis for the three conditions ZN, ON and HN, for occipital (Figure 7A-G) and C3 (Figure 7H-M) leads. We found that these levels of noise did not produce qualitative changes in the power spectra in electroencephalographic bands in the pre-stimulus time interval from -300 to 0 ms (see the map area between -300 to 0 ms in Figure 7); however, we found that during ON there is a statistically significant increase in the power amplitude for the VEP P100 around 100 ms (Figures 7B and 7F).

Discussion

In the present study we show for the first time that an individually determined optimal level of mechanical Gaussian noise in the frequency range, from 0 to 200 Hz, applied on the right index finger increases the mean amplitude of the P100 VEP, which was elicited by a well-known pattern-reversal visual paradigm. Our results show a multisensory SR phenomenon in the visual evoked potentials produced by the addition of mechanical noise on the finger. We found
the SR in the region overlying the primary visual cortical area but not in the region
overlying the somatosensory cortical area.

Comparison with earlier studies

In 1979 Harper discovered what is now termed: cross-modal stochastic
resonance (see Manjarrez et al., 2007), without even addressing occurrence of
“stochastic resonance”. In fact the term “stochastic resonance” was employed for
the first time by Benzi et al., in 1981, two years after the Harper’s publication.
Specifically Harper reported the inverted U-like increase on the sensitivity to visual
flicker produced by the addition of auditory white noise (Harper, 1979). Similar
psychophysical results with an inverted U-like increase were reported by our
research group when we employed auditory noise and the application of
subthreshold visual stimuli with a pair of LEDs (Manjarrez et al., 2007), and then
we employed for the first time the term “cross-modal stochastic resonance”. Later
Lugo et al., in 2008 examined the psychophysical effects of auditory noise in other
sensory modalities, thus confirming the observation of cross-modal stochastic
resonance. In the present study we decided to examine, by means of
electrophysiological experiments, what we term “multisensory stochastic
resonance in the brain P100 VEP”. We employed the checkerboard reversal
pattern visual paradigm instead of the LEDs visual stimulation because the
corresponding VEP elicited is very well defined with a clear positive peak showing
latency at around 100 ms, P100. Furthermore we employed tactile noise instead of
auditory noise.
Our electrophysiological results support the previous psychophysical report by Lugo et al., (2012), in which an effective tactile noise facilitates visual perception. In their work they concluded that tactile noise is capable of decreasing luminance modulation thresholds. To provide a theoretical explanation, these authors made use of the “fulcrum principle” (Lugo et al., 2008) which establishes that a subthreshold excitatory signal (of one sensory modality) that is synchronous with a facilitation signal (of a different sensory modality), can be increased up to a resonant-like level, and then decreased by the energy and frequency content of the facilitating signal. Namely, they suggested that the sensation of the signal changes according to the excitatory signal strength. Other investigations have tested the effect of simultaneous visuotactile stimulation on the activity of the human visual cortex. For example, Macaluso et al., 2000 showed that a sudden touch on one hand can improve vision in the neighboring space around that hand. In these experiments, tactile stimulation enhanced activity in the visual cortex, but only when it was on the same side as a visual target. Macaluso et al., 2000, suggested that touch influences unimodal visual cortex via back-projections from multimodal parietal areas. In other words, it was suggested that tactile information from the postcentral gyrus (i.e., contralateral somatosensory cortex) might thus be transferred to occipital areas (contralateral visual cortex) via back projections from parietal areas. This process would depend on whether the visual and tactile stimuli are on the same side.

Although visuo-tactile multisensory stochastic resonance could offer advantages for the improvement of visual signals it could also have some limitations for the correct functioning of other neural systems. Such is the case of
the vestibular system involved in the balance control in humans, in which tactile
noise can improve the balance (Priplata et al., 2002; Mulavara et al., 2011;
Magalhães and Kohn, 2011; see also Johannsen et al., 2015). For example,
Keshner et al. 2014 and Dettmer et al. 2015 demonstrated that balance
improvements by tactile noise are more pronounced with no vision available. In
particular, they demonstrated that the maintenance of postural control (even with
tactile noise added) is worse in an environment providing conflicting visual
information.

**Inter-individual differences**

We showed that all the subjects investigated exhibited inter-individual
differences in the optimal noise level and maximal P100 VEP amplitude during the
occurrence of multisensory SR. Such diversity of SR between subjects may be
attributed to their different sensitivity to stimuli. In psychophysical experiments,
discrepancies in individual sensitivity are explained by fluctuations in processes
such as fatigue, attention, expectancy, motivation, etc. Other possible causes for
inter-individual differences observed in the ON condition can be related to
dissimilarities in the configuration and orientation of the multiple “hotspots” in the
cutaneous receptive fields, the various receptor densities and afferent thresholds,
and differences in skin elasticity. In addition, fatigue, fluctuations in attention level,
arousal and top-down effects on the fusimotor drive may also play a role.
Differences could also occur with extremely slight changes in the orientation of
force on the fingertip. We cannot exclude the possibility that other nonspecific
physiological mechanisms are involved. These might include irregularity of the
background activity at the spinal, brainstem, thalamic and cortical levels (Manjarrez et al., 2002), which may explain the different profiles observed in the multisensory SR graphs obtained from individual experiments (Figure 4A).

**Possible mechanisms of multisensory SR**

Our results show that tactile ON is accompanied by increased amplitude of the prominent VEP component i.e., P100, which has been linked to selective attention (Mangun and Hillyard 1990; Hillyard et al., 1995; Trenado et al., 2009). Possible explanation for this increase is that tactile ON enhances the sensitivity of cutaneous mechanoreceptors and proprioceptors. Another possible explanation is facilitation of the internal SR in the visual pathways, which enables a change from subthreshold activity into firing activity of multisensory neurons in the brain regions that integrate visual and tactile signals from the hand (see Gentile et al., 2011 and our Discussion section in Mendez-Balbuena et al., 2012). From a psychophysical perspective Lugo et al., (2012) hypothesized that the facilitation observed in their experiments might be associated with the simultaneous activation of multisensory neurons in different brain regions once the tactile noise enters. In the context of the fulcrum principle, visual sensitivity transitions represent changes from subthreshold activity into firing activity of multisensory neurons. Based on their psychophysical results Lugo et al., (2012) proposed that the fulcrum principle is a fundamental physical principle that underlies sensory processing. Our electrophysiological study also provides support to this idea.

Regarding the mechanisms involved in the multisensory SR that we observed in our experiments, it is tempting to speculate that the checkerboard
visual stimulus is activating a fraction of the groups of neurons receiving multisensory inputs from tactile and visual pathways (see Figure 8A). It is possible that many of these neurons are in subthreshold conditions (see circle within the horizontal box in Figure 8B), thus strongly contributing to the multisensory SR observed in our experiments. In other words, we could attribute the increase of the P100 VEP amplitude to the SR generated by the existence of these subthreshold neurons in the multisensory tactile - visual pathways.

It is tempting to speculate that the VEP P100 component was the only significantly influenced by ON because a possible cross-modal interaction is occurring at the level of the superior colliculus, where multisensory neurons receive the visual and tactile information and send it to the striatal cortex to produce an amplified VEP P100. This could be the potential physiological mechanism that produces the facilitation of the VEP P100 signal for ON during the stochastic resonance in the superior colliculus.

**Possible applications in neuropsychology**

Our research suggests that the multisensory stochastic resonance involving tactile noise could be employed in vision rehabilitation as well as in the treatment of visuomotor disorders associated with low amplitude P100 VEPs. Our present study as well as other studies published by Lugo et al., 2012; Mendez-Balbuena et al., 2012; Trenado et al., 2014a,b and Malacuso et al., 2000 suggest that in the near future it will be possible to develop and to design new devices that enable the use of multisensory SR in the visuotactile modality for human sensorimotor enhancement and rehabilitation purposes. For instance, Mendez-Balbuena et al.,
2012, and Trenado et al., 2014a, suggested that multisensory SR could be employed to improve visuomotor human performance in easy non-invasive ways. This specific use of tactile noise could lead to the creation of wearable technologies. Furthermore, Lugo et al., 2012 suggested that the fulcrum principle may be the basis for explaining certain aspects of arousal dynamics related with the Yerkes–Dodson law (Yerkes and Dodson, 1908), in which multimodal SR can be applied in neuropsychological paradigms. Another possible scenario to exploit the multisensory SR is in Parkinson’s disease. It has been reported that stochastic vibrations applied to lower limbs of subjects with Parkinson enhances the mobility and decreases tremors in the same anatomical part where the vibration was applied (Haas, 2008; see also Samoudi et al., 2012; Trenado et al., 2014b).

Recently, we reported that in healthy humans the finger motor-timing in a time reproduction task is improved during an optimal level of auditory noise (De la Torre-Valdovinos et al., 2015). Based on such study and in the present results we predicted that an auditory, visual or tactile level of ON will improve the motor-timing in Parkinson Disease PD patients. A recent study by Hove and Keller (2015) supports our hypothesis. The authors report that PD patients’ gait improves when they walk with an auditory metronome or music. Therefore, a treatment approach that employs auditory, tactile or visual noisy cues could help optimize rhythmic sensory cues for treating motor and timing impairments in PD patients.

Recently, Samoudi et al., 2012 showed that the application of noisy galvanic vestibular stimulation promotes GABA release in the substantia nigra and improves locomotion in hemiparkinsonian rats. It is tempting to speculate that combined
multisensory noise sources could also be employed to improve locomotion in PD patients.

Moreover, potential applications of tactile noise could be also considered in the neuropsychological and neurophysiological fields; for example in the case of learning disabilities, attention deficit hyperactivity disorder (ADHD) and control of balance (Söderlund et al., 2007, 2010; Helps et al., 2014; Jaekl et al., 2014; Liu et al., 2013; Magalhães and Kohn, 2011, 2012; Baldan et al., 2014; see also Davis and Plaisted-Grant, 2015), as well as in age-related neurodegenerative diseases (Hass, 2008). Focusing on ADHD, Söderlund et al., 2007, 2010 (see also Helps et al., 2014) showed that noise has the potential to exert a positive effect as demonstrated by contrasting ADHD sufferers and controls that performed high memory and verbal tasks under the presence of auditory noise. At the behavioral level, such findings led to the hypothesis that ADHD sufferers are somehow under-stimulated with respect to their environment so they tend to look for external stimuli that results in distractibility. By the principles of stochastic resonance, such cognitive under-stimulation may be overcome when introducing noise to the perceptual system which enhances multisensory integration and attention towards specific stimuli. The present work is in line with the positive effect of ON in modulating (increasing the amplitude) the P100 VEP component, which has been implicated as a neural correlate of selective focal attention (Mangun and Hillyard, 1990; Luck et al., 1993; Heinze et al., 1994; Di Russo and Spinelli, 1999).

Conclusions
The present investigation demonstrates the electrophysiological occurrence of multisensory SR in the human visual pathway elicited by tactile noise. Our data extends the psychophysical experiments by Lugo et al., (2012) and Mendez-Balbuena et al., 2012 into the context of an EEG paradigm. These results show that tactile noise applied on the index finger could potentially modulate the amplitude of a relevant VEP component (P100) by following the principles of the multisensory SR phenomenon.
References


Figure legends

Figure 1. Input-output curves of visual stimuli versus VEP amplitude. (A) Checkerboard pattern reversal stimulation with different numbers of squares: 4, 16, 32, 64, 256 and 1024 as indicated. (B) P100 visual evoked responses to the checkerboard pattern reversal stimulation illustrated in A (60 clean trials averaged). The traces were obtained from the occipital electrode (O2). (C) The same as B but for the evoked potentials recorded in C3. (D) Input-output curves for the P100 VEP amplitude as a function of the number of squares in the checkerboard (mean±SE). (E) The same as D but for the evoked potential (EP) amplitude measured at 100 ms in C3. Figures D and E were normalized relative to the maximal P100 VEP illustrated in D.

Figure 2. Experimental setup. (A) The visual stimuli consisted of a visual pattern reversal paradigm (presentation of a checkerboard pattern changing every 0.5 s with a cross as a fixation point). (B) EEG was recorded from O1, OZ, O2 and C3 positions accordingly to the 10/20 system. (C) Continuous mechanical noise was applied on the right index finger. The output of a noise generator provided input to an indenter, namely a closed-loop mechanical stimulator–transducer that allowed measures of the force and displacement of the applied noisy stimuli. We maintained the intensity of the continuous tactile input noise constant for each “set of trials” and varied it between them (see methods). (D) Spectral power of the tactile stimuli: white noise (bandwidth 0-200 Hz). (E) Histogram of the mechanical noise applied to the right index finger. Note the Gaussian distribution of this noise. (F, G and H) Upper panel illustrates recordings of the applied noise: Zero noise
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(ZN), optimal noise (ON) and high noise (HN) as indicated. Lower panel shows the corresponding visual evoked potentials (VEP) for the three conditions.

**Figure 3. Averaged VEPs recorded on the occipital region for all the subjects (S1 to S8), for the three conditions: (A) Zero Noise (ZN), (B) Optimal Noise (ON) and (C) High Noise (HN).** The VEP was recorded in the channel for which the largest amplitude was found (O1, OZ or O2) as indicated. The transition of the pattern reversal stimuli is indicated by the checkerboard. The base line (0 µV) of the VEP for each subject is shown by an upper dotted line. The lower second dotted line is employed to illustrate the increase of the P100 VEP amplitude with respect to ZN condition. All subjects show an increase in the P100 VEP amplitude during ON.

**Figure 4. Occurrence of multisensory SR in occipital regions.** (A) Each graph was calculated from the P100 component of VEP recorded from the region overlying the primary visual cortex (O1, OZ or O2). Data were collected from all the subjects (8). All plots were typical of multisensory SR behaviour. Within a particular range of input tactile noises, the amplitude distributions of the P100 VEP were inverted U-like functions of the input noise. Note the inter-individual differences in the P100 VEP amplitude for the noise levels. The numbers inside the circles correspond to the subjects. (B) Pooled data for the amplitude of the P100 VEP. Individual values are shown for ZN, ON and HN. Note the significant higher amplitude of the P100 VEP for ON than for ZN and HN (asterisk).

**Figure 5. Averaged VEPs recorded on the C3 region for all the subjects (S1 to S8), for the three conditions: (A) Zero Noise (ZN), (B) Optimal Noise (ON) and**
(C) High Noise (HN). The same as Figure 2 but for C3. In all the subjects no
significant changes were observed in the amplitude of the “VEP” component at 100
ms for ON respect to the ZN condition. In fact in this region C3 there was an
absence of a P100 VEP.

**Figure 6. Absence of multisensory SR in C3 region.** The same as Figure 3 but
for C3. This could be considered as a control experiment. Note the absence of
multisensory SR. This finding supports the idea that the multisensory SR we found
for the visuotactile interactions is not an EEG artefact. NS, non-significant
parametric one-way repeated-measures ANOVA test.

**Figure 7. Time-frequency graphs for the peri-stimulus P100 VEP in the three
conditions ZN, ON and HN.** (A-C) Time-frequency graphs for the occipital leads.
(H-J) Time-frequency graphs for the C3 lead. (D-G) Grand average of the P100
VEP for the occipital regions. (K-M) Grand average of the P100 VEP for the C3
regions.

**Figure 8. Simplified neuronal model of multisensory SR in the visual
pathway.** (A) Scheme of a representative multisensory neuron in the visual
pathway activated by the simultaneous application of visual pattern reversal and
tactile noise. (B) An ensemble of many multisensory neurons (circles) receives
afferent inputs from visual and tactile pathways. Only a percentage of this
population are in subthreshold conditions (circle within the horizontal box). These
neurons will reach the threshold of action potential generation only when the
synaptic potentials elicited by the tactile noise and the visual input reach this
threshold. As a consequence, during ON this set of neurons contribute to increase the output response (i.e., the P100 VEP amplitude).

Table 1. Noise magnitude measured in displacement and force.
Experimental Setup

A. Visual Stimuli
- $f_s = 2$ Hz

B. Tactile Noise
- EEG
- Synamps 2

Tactile Noise

D. Power (mN²)
- Frequency (Hz)

E. Counts
- Noise (mN)

Effect of tactile noise on VEPs

F. Zero Noise (ZN)
G. Optimal Noise (ON)
H. High Noise (HN)

VEP (ZN) VEP (ON) VEP (HN)

Amplitude of P100 VEP
P100
<table>
<thead>
<tr>
<th>Subject</th>
<th>Noise Level</th>
<th>Displacement (mm)</th>
<th>Force (mN)</th>
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<td>2.15</td>
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<tr>
<td></td>
<td>HN</td>
<td>0.41</td>
<td>3.50</td>
</tr>
<tr>
<td>2</td>
<td>ON</td>
<td>0.41</td>
<td>1.80</td>
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<tr>
<td></td>
<td>HN</td>
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<td>3.10</td>
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<tr>
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