

## Review Article

# Clinical Implication of Auditory Evoked Potential Related with Sensitivity and Impulsivity

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## Abstract

The loudness dependence of the auditory evoked potential [LDAEP] is a measure of brain sensitivity and a potential biological marker of central serotonergic activity. Serotonin was also known to be related with impulsivity. Hence, LDAEP may be useful to evaluate a relationship between sensory sensitivity and impulsivity. As has been reported, LDAEP is related to depression, anxiety and mood lability in clinical samples as well as healthy participants, because patients with high emotional sensitivity often report somatosensory sensitivity, and show higher sensory arousal responses, reflected by LDAEP. Certain clinical populations may also show deviant LDAEPs modulated by pathological impulsivity traits. Clinical populations with abnormal impulsivity often show faster reaction times for motor responses and elevated false alarm rates in a response inhibition task, and likely represent an abnormal serotonergic expression. Hence, LDAEP appears to be a marker of impulsivity with the changes of inhibitory behavioral properties. Functional neuroimaging studies additionally support our arguments, because impulsivity-related inhibition performances are associated with activation of prefrontal cortex, one of representative areas for a serotonergic system. In summary, LDAEP may significantly function as a promising biological marker for reflecting sensitivity and impulsivity in not only clinical but also general populations.

## Keywords

- Sensitivity
- Impulsivity
- Auditory evoked potential
- Mental disorder

## INTRODUCTION

The loudness dependence of auditory evoked potentials [LDAEP] is recently regarded as a valid marker of the central serotonergic activity. LDAEP is inversely associated with a central serotonergic activity, with high LDAEP reflecting low levels of serotonergic neurotransmission [1]. The LDAEP was calculated as the amplitude change of the evoked N1/P2 components in response to different auditory stimulus intensities [1]. Regarding the process of getting LDAEP, the sensitivity to auditory stimulus could affect the strength of LDAEP. Additionally, considering the fact that LDAEP reflects the central serotonin activity, several researchers have studied the relationship between LDAEP and emotional component of sensitivity.

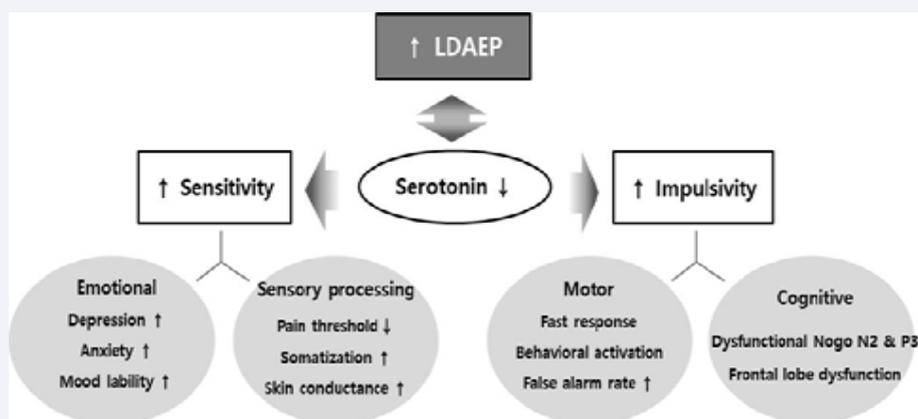
Impulsivity has been defined as the inability to inhibit an inappropriate behavior [2] and regarded as the clinical aspects of poor behavioral response inhibition [3]. Many previous studies reported that a serotonin system plays a critical role for behavioral inhibition and impulsivity [4-6]. Dysregulation of serotonin systems in sub-regions of the prefrontal cortex has been implicated in impulsivity [7]. Considering the associations between impulsivity and central serotonin system, the possibilities of LDAEP reflecting impulsivity can be predicted.

Both sensitivity and impulsivity have great impact on the mental illness. The relationship between sensory sensitivity and impulsivity might be different in various clinical populations and it has not been conclusive. However, it seems to be existed obvious relationship between sensitivity and impulsivity with serotonin systems as a mediator. Making LDAEP as a candidate of clinical marker for sensitivity and impulsivity could be an important issue which deserves a greater clinical attention.

In this article, we inquire the clinical implication of auditory evoked potential related to sensitivity and impulsivity by the review of the previous study results. We focus on two themes underlying our hypothesis (Figure 1): 1] relationship between LDAEP and sensitivity associated with sensory and emotional component, and 2] relationship between LDAEP and impulsivity associated to motor and cognitive inhibition.

## LDAEP and sensitivity

**LDAEP and emotional sensitivity:** Aron and Aron [8] declared the concept of sensory processing sensitivity [SPS], and made the highly sensitive person's scale [HSPS]. The HSPS had large positive correlations with emotionality [8]. Emotionality was measured by items related to worry, fear and depression [8]. Moreover, there is some evidence that people higher in SPS have



**Figure 1** LDAEP could reflect sensitivity and impulsivity, both have shared the serotonin related regulation. LDAEP might be correlated with the emotional sensitivity and sensory processing sensitivity. Moreover, LDAEP would be correlated with impulsivity, which would cover motoric and cognitive factors.

stronger emotional responses overall [9]. It has been found to be related to social phobia [10], anxiety and depression [11], and agoraphobic avoidance [12]. Meanwhile, clinical studies reported that the changes of LDAEP value in mental disorders are related to emotional sensitivity such as major depressive disorder, bipolar disorder and general anxiety disorder [13-15]. In the studies, patients with atypical depression [i.e., rejection sensitivity and labile mood] had higher LDAEP values [15] and the LDAEP value of patients with bipolar disorder varied according to current mood status [14]. Lee et al.'s study [16] revealed that LDAEP was significantly related to the mood reactivity in patients with major depressive disorder. Furthermore, our study results showed that higher LDAEP had higher depression, anxiety and mood lability scores in healthy participants [Kim et al., submitted]. It suggests that the level of LDAEP is closely related with the emotional sensitivity and mood reactivity in healthy participants as well as clinical samples.

**LDAEP and sensory processing sensitivity:** SPS is a temperament/personality trait characterized by sensitivity to both internal and external stimuli, including social and emotional cues [17]. They declared the concept of SPS, and made the HSPS [8]. The HSPS measures sensitivity with items including being aware of subtleties, bothered by intense stimuli and strongly affected by caffeine, pain, hunger and loud noises [8,17,18]. Additionally, a highly sensitive person is more prone to arousal, especially after exposure to sense stressors such as bright lights, loud noise and strong smells [19,20]. Highly sensitive human babies have shown higher heart rates compared to controls [21].

Regarding that SPS is associated with clinical states such as depression and anxiety, as described above, it could be hypothesized that participants with high emotional sensitivity show higher sensory responses. In a clinical study, women with panic disorder exhibited greater skin conductance magnitudes and endorsed more severe menstrual symptoms relating to bodily sensations, anxiety sensitivity, state and trait anxiety, fear of body sensations, and illness-related concerns [22]. Additionally, patients with anxiety and depression related mental disorders such as panic disorder and post-traumatic stress disorder reported higher pain sensitivity, skin conductance or somatic sensations [23-26].

Meanwhile, the previous study reported that auditory sensory gating measured by P50 response, as another index of sensory sensitivity impaired in patients with antisocial personality disorder showing higher impulsivity [27,28]. It suggests that clinical population with impulsivity shows low sensitivity to stimuli. On the other hand, healthy population with higher impulsivity showed better sensory gating [27]. It seems that the relationship between impulsivity and sensitivity is different in various populations.

Considering that the LDAEP could be a marker for sensitivity, there might be a direct relation between LDAEP and sensory sensitivity such as pain threshold, somatic response and skin conductance. However, there has been no study evaluating the relationship between LDAEP and sensory sensitivity. Further studies would be needed to assess the association.

## LDAEP AND IMPULSIVITY

Impulsivity has been defined as the inability to inhibit an inappropriate behavior, acting without thinking, acting prematurely and inappropriately to a situation with undesirable consequences, or as an aversion to wait [29]. Regarding that the serotonin plays a role in behavioral inhibition [30] and that LDAEP can be an indicator of central serotonin activity, LDAEP could be associated with response impulsivity.

### LDAEP and motor inhibition

Previous studies reported that ERP of the Go/Nogo tasks was associated with response inhibition and impulsivity [31-33]. Impulsivity is a tendency to make rapid decisions and act on the spur of the moment [34]. From the definition of impulsivity, as described above, it could be hypothesized that high impulsive subjects would have shorter reaction times and make many errors in the Go/Nogo task. With this hypothesis, several previous studies reported that participants showing impulsive tendency or clinical samples showed faster reaction time and more false alarm rates [error rates] in the task [35,36].

Additionally, impulsivity itself has been regarded as a complex trait-cluster and behavioral activation system [BAS] related trait [37,38]. The BAS system would be activated when subjects face conditioned positive stimuli and signals of

nonpunishment, resulting in approach behaviours [39]. Gray [40] suggested that individual differences in BAS activation give rise to impulsivity. Participants with higher internet addiction inventory scores showed faster response times in the Go/Nogo task [41]. Moreover, the BAS scores were related to scores of internet addiction inventory and they were predictive of reaction time [41]. It suggests that behavioral activation is also related to motor inhibition in the Go/Nogo task.

Previous studies revealed that increased false alarm rates of Nogo trials could be related to the low serotonin function and genetic mutation of serotonin system [42,43]. These evidences show that the serotonin plays a core role in Nogo performances reflecting motor inhibition [30]. Our study reported that the higher LDAEP group showed higher false alarm rates in the Nogo trial [Kim et al., submitted]. LDAEP appears to be related with motor inhibition.

### LDAEP AND INHIBITION-RELATED NEUROPHYSIOLOGICAL RESPONSES

Because inhibition is a covert process, cognitive neuroscience techniques such as ERP and functional magnetic resonance imaging [fMRI] are increasingly being used to explore these hidden processes of inhibition [44].

In the Nogo trials, the N2 and P3 component have been linked with the process of response inhibition [45,46]. Especially, the Nogo P3 amplitude was related to impulsivity [47-49]. Hartman et al., [50] insisted that the diminished Nogo P3 might be an indicator for poor response inhibition. In contrast, Dong et al., [48] reported that the people with internet addiction disorder exhibited higher Nogo-P3 amplitude than controls. In our study conducting in healthy participants, LDAEP was positively correlated with Nogo P3 amplitude and Nogo-P3 amplitude was significantly higher in the high LDAEP group compared to the lower LDAEP group [Kim et al., submitted]. It suggests that LDAEP could be a marker reflecting impulsivity with the Nogo P3 changes. Moreover, the results of source analysis of the Nogo N2 and P3 showed a decreased activation in the frontal lobe especially, prefrontal cortex [PFC] such as dorsolateral PFC, orbitofrontal cortex, inferior and medial frontal cortex and anterior cingulate cortex in participants with poor impulse control [31,42,51-53].

Meanwhile, neuroimaging studies showed that impulsivity and inhibitory control are regulated by the function of the prefrontal cortex [PFC] [54]. Previous fMRI analyses of the Go/Nogo task have shown that successful inhibition trials are associated with an increased activation PFC including the right dorsolateral PFC, ventrolateral PFC, precentral gyrus and anterior cingulate cortex [34,55-57].

Taken together, LDAEP is associated with a cognitive inhibition, which is a component of impulsivity with changes of Nogo-N2 and P3 amplitudes and prefrontal activation.

### CONCLUSION

Both sensitivity and impulsivity are important psychological trait in human nature and play a critical role in the social relation and mental disorders. Accumulating evidence showed that LDAEP could be related to emotional and sensory processing

sensitivity. Additionally, LDAEP reflects impulsivity associated with motor and cognitive inhibition. The LDAEP, an auditory evoked potential could be a promising biological marker for reflecting both sensitivity and impulsivity not only for clinical population but also for general population.

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