



Letter to the editor

Spontaneous eye blink in patients with psychosis in perceptions of stimulus salience



Dear Editors,

Previous studies have noted that spontaneous blink rate (SBR) could reflect the central dopaminergic activities in our brains (Chan et al., 2010; Karson, 1983). SBR has been adopted as a proxy clinical measure for dopamine activity as it is less costly and invasive than positron emission tomography (PET) radiotracer neuroimaging technique (Chan et al., 2010). Elevation of resting dopaminergic activity was observed in schizophrenia (Chen et al., 1997) regardless of antipsychotic medication treatment (Chen and Hui, 2000; Karson, 1983; Mackert et al., 1990; Stevens, 1978). While Horvitz (2000) proposed an increase in dopaminergic activity under salient conditions, reduced SBRs were found in visual salient stimuli in healthy participants (Nakano et al., 2009; VanderWerf et al., 2003), so as to prevent the loss of significant information during eye blinking. Therefore, it is postulated that salient stimuli that are presented auditorily would result in heightened dopamine activity and may also be a more direct representation of true dopaminergic level than visual stimuli. As some symptoms of the psychosis, e.g., delusion and hallucination, are caused by a dysregulated central dopaminergic system (Bennett, 1998; Carlsson et al., 2001; Kapur, 2003; Kasper, 2002; Roberts, 1992), we examined the difference in salient ratings and corresponding SBRs under exposure to auditory salient stimulus between psychosis patients and healthy participants and those between patients with and without active psychotic symptoms.

This cross-sectional study included adult (age 18–64 years), Cantonese-speaking Chinese psychotic patients from outpatient psychiatric units at the Queen Mary Hospital and the Western Psychiatric Center of Hospital Authority in Hong Kong. Psychosis is defined by a DSM-IV diagnosis of schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, brief psychotic disorder, psychotic disorder not otherwise specified, or manic episodes with psychotic features. Patients who had known neurological condition, movement disorders, learning disability, and substance abuse were excluded. Healthy participants were age- and gender-matched and had no previous history of mental illness or use of antipsychotics and no family history of psychotic illness. All participants that had eye illness causing local irritation, history of eye surgery impacting cornea, or use of ocular topical anesthetic agent in preceding seven days were also excluded. The study had been approved by the institutional review board and ethics committee of the applying site.

Participants' basic demographic information, clinical presentation (for patients only, including positive symptoms, negative symptoms, extrapyramidal side effects and involuntary movement) and cognitive functioning were assessed by trained researchers. Participants' eye

blinks assessed between 10:00 am and 5:00 pm to avoid tiredness and were videotaped while they were listening to a 6-minute story that served as the auditory salient stimulus while looking at a computer screen that showed a peaceful aquarium scene. The story has nine paragraphs, and each with its own theme. After the story has finished, they were asked to recall the story to ensure they had paid attention. They also rated the salience level in each paragraph; ranging from 0 (not salient), 1 (salient), to 2 (highly salient). SBRs were then counted by an automated computer program and cross-validated manually by researchers.

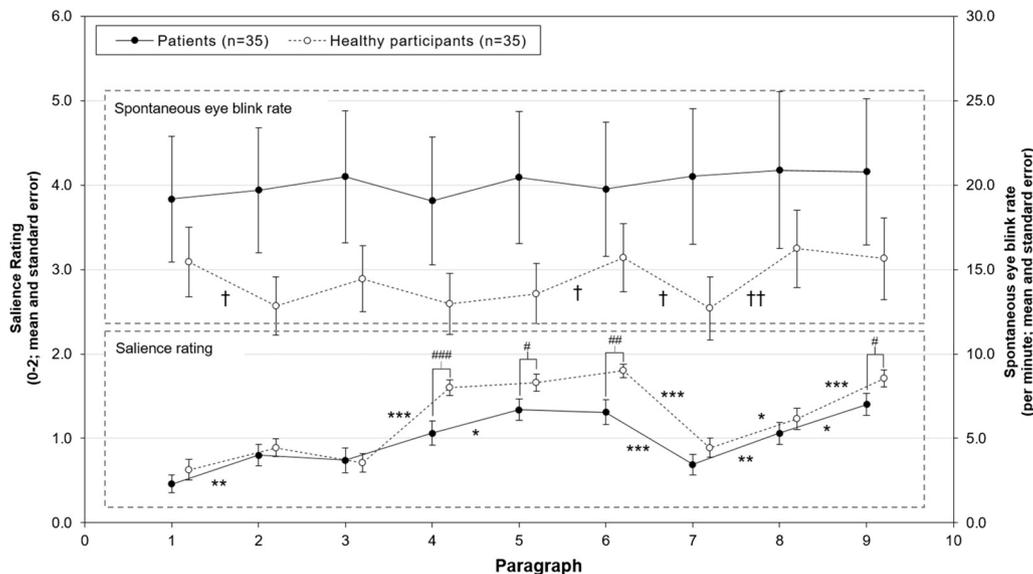
Repeated measure ANOVAs were conducted to test the overall differences of salience rating and SBRs across nine and between two consecutive paragraphs (i.e., 1 to 2, 2 to 3, 3 to 4, and so on) between patients and healthy subjects. ANCOVA were used to test the differences in salience ratings and SBRs between patients and healthy subjects with adjustment for years of education. Patients with active psychotic symptoms (any SAPS subscale global score > 2) and those without (all SAPS subscale global scores ≤ 2) were further compared using same statistical methods with SAPS and dosage of antipsychotic medication adjusted in ANCOVA.

Thirty-five psychosis patients and their matched healthy participants were recruited and the latter had received more years of education ($p = 0.005$) (Supplementary Material 1). 20 patients were with active psychotic symptoms while 15 were not. They were demographically similar except that patients with active psychotic symptoms had received significantly higher dosage of antipsychotic medication ($p = 0.005$) and more severe positive symptoms ($p < 0.001$) than those without active symptoms.

Comparing with the patients, healthy participants had significantly higher salience ratings in paragraphs 4, 5, 6 and 9. Both groups had significant drop in their salience ratings from paragraph 6 to 7 and increase from 7 to 8 and 8 to 9. Increase was also observed from paragraph 1 to 2 and 4 to 5 in patients and 3 to 4 in healthy participants. SBRs were similar between the two groups while significant increase was observed from paragraph 5 to 6 and 7 to 8 while drop from 6 to 7 in healthy participants (Fig. 1). No significant difference was found in both salience ratings and SBRs between patients with and without active psychotic symptoms. Both groups had a significant drop in salience rating from paragraph 6 to 7 while patients without active psychotic symptoms had a significant increase from 8 to 9. No significant differences in SBRs were observed between the two patient groups and between paragraphs in each group (Supplementary Material 2).

Using SBR as a potential behavioral marker for central dopaminergic activity, this study compared SBRs under an auditory salient stimulus (story telling) in psychosis patients and healthy subjects, while most previous studies examined only the resting SBR in psychotic disorders (Chan et al., 2010; Chan and Chen, 2004; Chen and Hui, 2000; Mackert et al., 1990). As expected we found patients have lower overall salience ratings on the story than controls. However, we did not find a higher SBR in patients than healthy controls under exposure to auditory salient stimulus.

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Comparison of salience ratings between groups adjusted for years of education: $^{\dagger}p<.05$, $^{\dagger\dagger}p<.01$ & $^{\dagger\dagger\dagger}p<.001$.
 Comparison of salience ratings between paragraphs in the same group: $^{\ast}p<.05$, $^{\ast\ast}p<.01$, and $^{\ast\ast\ast}p<.001$.
 Comparison of SBRs between paragraphs in the same group: $^{\dagger}p<.05$, $^{\dagger\dagger}p<.01$, and $^{\dagger\dagger\dagger}p<.001$.

Fig. 1. Salience ratings and spontaneous eye blink rate in patients and healthy participants.

To further investigate the use of SBR, studies could be conducted in patients at different stages of psychosis, namely first episode psychosis, relapse, and medication-naïve, to explore whether there would be any difference in spontaneous eye blink patterns. Another direction of research could be the potential effects of antipsychotics medication on SBR. The findings in this research gave further directions for incorporating SBR into other behavioral tasks for a better understanding of patients with psychotic disorders.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.schres.2019.05.029>.

Contributors

FYKT and EYHC designed the study and wrote the protocol. FYKT managed the literature searches and analyses. FYKT, YNS, CLMH and EYHC undertook the statistical analysis, and HWSY and YNS wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Declaration of Competing Interest

EYHC reports having received speaker honoraria from Otsuka and DSK BioPharma; received research funding from Otsuka; participated in paid advisory boards for Janssen and DSK BioPharma; received funding to attend conferences from Otsuka and DSK BioPharma. The remaining authors declare no competing interests.

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