Neurophysiological Correlates of WM Retrieval in Schizophrenia During a Serial Position Test with Words or Faces

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Abstract
The background related potential (ERP) ‘old/new’ effect (enhanced parietal positivity 300–800 ms after correctly recognized repeated items) is a reliable neurophysiological correlate of conscious recollection, which is reduced in schizophrenia during word but not face recognition (Kayser et al., 1999, 2009, 2010). This study examined whether the task-specificity of this effect also applies to WM retrieval. Methods: 67-channel ERPs were recorded from 75 schizophrenic patients and 64 healthy controls (right-handed) during a WM paradigm with words or faces. After sequentially encoding three items (600 ms, 1.5 s ISI), one item was repeated after a 3 s delay (probe), and its serial position was reported. Results: ERPs were transformed into reference-free current source density (CSD, spherical spline interpolation) wavefoms, which were more positive for probe (old) than encoding (new) items, revealing differences highly similar to recognition memory old/new effects. An unrestricted Veenstra-Voogd identified positive sources peaking at 281 ms (parietal/occipital) and 660 ms (cerebral). Although both groups performed well in the word task (>90% correct), probe/encode effects over left lateral parietal sites for the 660 ms were markedly reduced in patients. In contrast, probe/encode effects for this source were comparable in patients and controls for faces, despite poorer performance in patients (72±14.3% vs. 88±3.9%). Conclusions: The findings suggest that neurophysiological abnormalities of conscious recollection in schizophrenia are specific to tasks dependent on phonological encoding and/or semantic processing.

Keywords: Schizophrenia, working memory, conscious recollection, ERP, CSD-PCA

Introduction
Schizophrenia patients had significantly reduced WM performance compared to healthy controls for both words and faces (Kayser et al. 1999). Item repetition during serial position tests yielded robust probe/encode ERP effects that were highly comparable to ERP old/new effects typically observed during explicit recognition memory paradigms (Kayser et al. 2007). This finding contrasts with studies in schizophrenia that applied CSD and source analysis in patients and controls (Blaauw et al. 2007; Maquet et al. 1999). CSD analyses revealed similar early, and reduced late, probe/encode effects for words in schizophrenia compared to controls (Kayser et al. 1999). The notion of a phonological encoding deficit is in agreement with prior findings that reduced probe/encode effects were greater over the left than right hemisphere, implicating impaired conscious recollection of verbal material (Kayser et al. 2009). Because verbal information is readily stored in a phonological loop, healthy adults may have an advantage in accessing probe/encode effects for words over faces. In contrast, probe/encode effects were comparable in patients and controls for faces (Kayser et al. 2009).

Materials and Methods
Participants
The current study was part of a larger study on WM retrieval in schizophrenia (Kayser et al. 2007). Patients met DSM-IV-TR criteria for schizophrenia (Schneiderian first-rank symptoms, disorganization/insensitivity to social cues, a logical thought content). Controls had no history of any psychiatric disorder or neurology disorder. Patients (N = 75) and controls (N = 44) were recruited through local advertisements.

ERPs were recorded using an electrode cap (177 scalp sites, active recording reference (Biocap)). An active reference was selected by a 2-phase Proband and Global average reference filter (Perrin et al. 1989). Electrode impedances were below 5 kΩ. The analog signals were band-pass filtered (1–100 Hz), amplified (NWB,12-bit), and digitized at a sampling rate of 1000 Hz (NWB 12-bit). Signals were epoched from −1000 ms to 2000 ms. A total of 200 artifact-free trials (80%) were averaged for each participant. The raw data were imported into the Brain Vision Analyzer for further analysis (Munte et al. 2001). For all groups, a CSD analysis was conducted to quantify neuronal generator activity (Kayser et al. 2007). The CSD solutions were integrated with spherical splines (Perrin et al. 1989). Compensatory analyses were conducted to control for between-subjects factors (Kayser et al. 2007).

Behavioral Data
The recognition memory experiment was designed to measure patients’ and controls’ ability to identify which item had been presented during the previous encoding session (Kayser & Tenke 2003, 2006a, 2006b). Subjects were instructed to indicate whether each item was “old” or “new” by pressing a button with their right or left hand (Kayser et al. 1999). The probe/encode effect was calculated by subtracting the mean amplitude of the encoding epoch (i.e., 1 s before stimulus presentation) from the probe amplitude (i.e., 1 s after stimulus presentation). In order to control for the task difficulty, the probe/encode effect was standardized (Kayser et al. 2007). A reliable probe/encode effect was defined as an amplitude at the probe minus encoding epoch exceeding 0.04 μV/cycle (Kayser et al. 2007).

Conclusions
Because verbal information is readily stored in a phonological loop, healthy adults may have an advantage in accessing probe/encode effects for words over faces. In contrast, probe/encode effects were comparable in patients and controls for faces (Kayser et al. 2009).

Summary and Conclusions
The main finding of the current study is that probe/encode effects over left lateral parietal sites for the 660 ms were markedly reduced in patients. These findings suggest that neurophysiological abnormalities of conscious recollection in schizophrenia are specific to tasks dependent on phonological encoding and/or semantic processing.

References

Fig. 1. Mean (SEM) performance accuracy during the Serial Position Test (SPT), corrected by words or faces. A, asterisk, representing the encoding of probe items was more difficult for faces than words. B, Patients performed more poorly than controls (Group, p < .01; ***p < .001). Significant group main effects for each task at each epoch are indicated as follows: ***p < .001; **p < .01; *p < .05.

Fig. 2. Grand-mean CSD waveforms at parietal sites (P7, P3) for 44 healthy adults and 75 schizophrenia patients comparing words (top) or faces (bottom) presented during the encoding phase (new) and probe phase (old). Probe/encode effects (i.e., greater probes than correct probes) began at around 200–300 ms and were highly similar to the classical old/new effects identified in normal healthy adults. Whereas encode/old effects were clearly present in both groups over medial-parietal sites (P3) for words and faces, only controls revealed substantial probe/new effects at lateral parietal sites (P7).

Fig. 4. Mean (SDN) probe/encode effects for the late source (660) at lateral centroparietal sites, which were significantly larger in patients compared to controls (Group, p < .05; **p < .01). Across all conditions, probe/encode effects were greater for left than right hemisphere (Hemisphere, p < .05). Significant group main effects for each task and hemisphere (LH vs. RH) are indicated (SDN, p < .05).

Fig. 3. The unrestricted Veenstra-Voogd identified late sources peaking at 281 ms (19±5% explained variance) and 660 ms (15±5%), which accounted for most of the variance during the task interval times (p < .0001) in probe/encode effects. The source level correlation between both conditions (old/new vs. old/new) was highly significant across all conditions (p < .0001). Across all conditions, probe/encode effects were greater at lateral than medial sites for probe/encode effects at lateral parietal sites (P7).

Fig. 5. Mean (SEM) probe/encode effect for the late source (660) at lateral centroparietal sites, which were significantly larger in patients compared to controls (Group, p < .05; **p < .01). Across all conditions, probe/encode effects were greater for left than right hemisphere (Hemisphere, p < .05). Significant group main effects for each task and hemisphere (LH vs. RH) are indicated (SDN, p < .05).

Fig. 6. Percentage correct at each serial position (transposed to the Serial Position Test) for each task. The overall probe/encode effect was significant for each task (Wilcoxon test). Group, Task: p < .05 (Wilcoxon test). Significant group main effects for each task and hemisphere (LH vs. RH) are indicated (SDN, p < .05).